THE LANCET

Supplementary appendix

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Supplement to: Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. *Lancet* 2014; **383:** 1899–911.

Table S 1 Overview of codes used to define each cardiovascular endpoints and data sources. Details of how these codes are combined are given in the CALIBER data portal

Endpoint	CPRD – Read codes	MINAP – specific disease registry	HES – OPCS 4 hospital procedures	HES – ICD 10 hospital diagnoses†	ONS – ICD 10 causes of death‡
Stable angina	G33..00: Stable Angina G33z.00: Angina pectoris NOS + 19 other Read codes for diagnosis of stable angina pectoris. G33z400: Ischaemic chest pain Coded test results associated with 33 Read codes for coronary angiography or 139 Read codes for myocardial ischaemia tests (resting ECG, exercise ECG, stress echo, radioisotope scan) 57 Read codes for coronary artery bypass graft 28 Read codes for percutaneous coronary intervention Two or more successive prescriptions for anti-anginals.	nu	K40-K46: Coronary artery bypass graft. K49, K50 and K75: Percutaneous coronary intervention	I20.1: Angina pectoris with documented spasm I20.8: Other forms of angina pectoris I20.9: Angina pectoris, unspecified	nu
Unstable angina	G311500: Acute coronary syndrome G311100: Unstable angina + 10 other Read codes for unstable angina	Discharge diagnosis of acute coronary syndrome without raised troponin .	Lack of coronary artery bypass graft or percutaneous coronary intervention record in the same hospital spell as I20.9 implies admission for unstable angina	I20.0: Unstable angina. I24.0: Coronary thrombosis not resulting in MI. I24.8: Other forms of ischaemic heart disease. I24.9: Acute ischaemic heart disease, unspecified. 'I20.9: Angina pectoris, unspecified' without coronary artery bypass graft or percutaneous coronary intervention in the same hospital spell	nu
Coronary heart disease not otherwise specified	G3...00: Ischaemic heart disease + 29 other Read codes	nu	nu	I25 (CHD NOS, chronic ischaemic heart disease, silent MI) except 'I25.2: Old MI'	nu

Non-fatal acute Myocardial Infarction (MI)	G30X000: Acute ST segment elevation myocardial infarction. G307100: Acute non-ST segment elevation myocardial infarction. G30..15: MI Acute myocardial infarction + 53 other Read codes 7929100: Percut transluminal coronary thrombolysis with streptokinase + 3 other Read codes for coronary thrombolysis Elevated cardiac markers, troponin or CKMB results associated with 16 Read codes	MI with or without ST elevation based on initial ECG findings, raised troponins and clinical diagnosis.	K50.2: Percutaneous transluminal coronary thrombolysis using streptokinase K50.3: Percutaneous transluminal injection of therapeutic substance into coronary artery NEC	I21: Acute MI. I22: Subsequent MI	nu
Unheralded coronary death	Any CVD excluded.	Any CVD excluded.	Any CVD excluded.	Any CVD excluded.	I20-I25: Ischaemic heart disease
Heart failure	G58..00: Heart Failure + 40 other Read codes for heart failure 585f.00: Echocardiogram shows left ventricular systolic dysfunction 585g.00: Echocardiogram shows left ventricular diastolic dysfunction	nu	nu	I11.0: Hypertensive heart disease with (congestive) heart failure I13.0: Hypertensive heart and renal disease with (congestive) heart failure I13.2: Hypertensive heart and renal disease with both (congestive) heart failure and renal disease I50: Heart failure	I11.0 Hypertensive heart disease with (congestive) heart failure I13.0: Hypertensive heart and renal disease with (congestive) heart failure I13.2: Hypertensive heart and renal disease with both (congestive) heart failure and renal disease I50 Heart failure
Ventricular arrhythmias, cardioversion, cardiac arrest and sudden cardiac death	G757.00: Cardiac arrest + 30 other Read codes for ventricular fibrillation, asystole, cardiac arrest, cardiac resuscitation G575100: Sudden cardiac death, so described	nu	X50: External resuscitation. K59: Cardioverter defibrillator introduced through the vein	I46.0: Cardiac arrest with successful resuscitation I46.1: Sudden cardiac death, so described I46.9: Cardiac arrest, unspecified I47.0: Re-entry ventricular arrhythmia I47.2: Ventricular tachycardia I49.0: Ventricular fibrillation and flutter	I46.0: Cardiac arrest with successful resuscitation I46.1: Sudden cardiac death, so described I46.9: Cardiac arrest, unspecified I47.0: Re-entry ventricular arrhythmia I47.2: Ventricular tachycardia I49.0: Ventricular fibrillation and flutter

Transient ischaemic attack	G65..12: Transient ischaemic attack + 5 other Read codes	nu	nu	G45.8-G45.9: Transient cerebral ischaemic attack	nu
Ischaemic stroke	G64..11: CVA – cerebral artery occlusion + 9 other Read codes 7A20311: Carotid endarterectomy and patch + 4 other Read codes for carotid endarterectomy within 90 days of stroke not otherwise specified denote ischaemic stroke	nu	L29.5: Endarterectomy of carotid artery NEC + 3 other codes for carotid endarterectomy or stenting within 90 days of stroke not otherwise specified denote ischaemic stroke	I63: Cerebral infarction.	I63: Cerebral infarction.
Stroke not otherwise specified	G66..00: Stroke and cerebrovascular accident unspecified + 14 other Read codes	nu	U54.3 Delivery of rehabilitation for stroke	I64: Stroke, not specified as haemorrhage or infarction G46.3-G46.7: Stroke syndromes	I64: Stroke, not specified as haemorrhage or infarction I67.2: Cerebral atherosclerosis I67.9: Cerebrovascular disease, unspecified
Subarachnoid haemorrhage	G60X.00: Subarachnoid haemorrh from intracranial artery, unspecif + 2 other Read codes for subarachnoid haemorrhage	nu	Nu	I60: Subarachnoid haemorrhage.	I60: Subarachnoid haemorrhage.
Intracerebral haemorrhage	G61..00: Intracerebral haemorrhage + 16 other Read codes for intracerebral haemorrhage.	nu	nu	I61: Intracerebral haemorrhage.	I61: Intracerebral haemorrhage.
Peripheral arterial disease	63 codes for Lower limb peripheral arterial disease diagnosis (including diabetic PAD, gangrene and intermittent claudication). 136 Read codes for peripheral arterial disease procedures 2 Read codes for abnormal lower limb angiogram	nu	L50-L54: Bypass, reconstruction and other open operations on iliac artery. L58-L60, L62: Bypass, reconstruction, transluminal operations or other open operations of femoral artery. L65: Revision of reconstruction of artery.	I73.1: Thromboangiitis obliterans I73.8: Other specified peripheral vascular diseases I73.9: Peripheral vascular disease, unspecified I74.3: Embolism and thrombosis of arteries of lower extremities I74.4: Embolism and thrombosis of arteries of extremities, unspecified I74.5: Embolism and thrombosis of iliac artery	I73.1: Thromboangiitis obliterans I73.8: Other specified peripheral vascular diseases I73.9: Peripheral vascular disease, unspecified I74.3: Embolism and thrombosis of arteries of lower extremities I74.4: Embolism and thrombosis of arteries of extremities, unspecified I74.5: Embolism and thrombosis of iliac artery

Abdominal aortic aneurysm	G714.00: Abdominal aortic aneurysm without mention of rupture + 12 other Read codes	nu	L18: Emergency replacement of aneurysmal segment of aorta L19: Other replacement of aneurysmal segment of aorta L20: Other emergency bypass of segment of aorta L254: Operations on aneurysm of aorta NEC L27: Transluminal insertion of stent graft for aneurysmal segment of aorta L28: Transluminal operations on aneurysmal segment of aorta	I71.3: Abdominal aortic aneurysm, ruptured I71.4: Abdominal aortic aneurysm, without mention of rupture I71.5: Thoracoabdominal aortic aneurysm, ruptured I71.6: Thoracoabdominal aortic aneurysm, without mention of rupture I71.8: Aortic aneurysm of unspecified site, ruptured I71.9: Aortic aneurysm of unspecified site, without mention of rupture	I71.3: Abdominal aortic aneurysm, ruptured I71.4: Abdominal aortic aneurysm, without mention of rupture I71.5: Thoracoabdominal aortic aneurysm, ruptured I71.6: Thoracoabdominal aortic aneurysm, without mention of rupture I71.8: Aortic aneurysm of unspecified site, ruptured I71.9: Aortic aneurysm of unspecified site, without mention of rupture

Note: AAA, aortic abdominal aneurysm; MI, myocardial infarction; nu = not used in definition.

†Primary cause of admission.

‡Underlying cause of death.

Table S 2 Cohort summary characteristics[1,2,3].

	SBP <115 & DBP <75 mmHg	SBP 115-139 or DBP 75-89 mmHg	SBP 140-159 or DBP 90-99 mmHg	SBP >160 or >100 mmHg
N patients	202,435	638,658	313,748	103,165
Age, years	38.7 (10.0)	44.9 (13.6)	56.4 (15.0)	63.9 (14.5)
Female sex	155,617 (76.9%)	362,678 (56.8%)	156,672 (49.9%)	57,690 (55.9%)
White ethnicity	99,397 (84.4%)	322,704 (88.9%)	173,824 (93.1%)	60,237 (95.2%)
Most deprived quintile	42,342 (20.9%)	127,486 (20.0%)	60,446 (19.3%)	21,164 (20.5%)
Smoking status[4]				
Ex-smoker	26,524 (15.1%)	92,996 (16.9%)	51,381 (19.8%)	14,266 (17.9%)
Current smoker	43,814 (24.9%)	129,724 (23.6%)	47,217 (18.2%)	12,053 (15.1%)
Medical history				
Diabetes	1,907 (0.9%)	20,198 (3.2%)	17,685 (5.6%)	5,912 (5.7%)
Kidney disease	1,593 (0.8%)	7,215 (1.1%)	4,679 (1.5%)	1,280 (1.2%)
COPD	1,773 (0.9%)	9,436 (1.5%)	7,847 (2.5%)	3,121 (3.0%)
Measurements[4]				
Body mass index, kg/m^2	23.1 (21.1-25.7)	25.6 (22.9-28.8)	27.3 (24.4-30.9)	27.5 (24.4-31.2)
Total cholesterol, mmol/L	5.0 (4.3-5.7)	5.2 (4.5-6.0)	5.4 (4.7-6.2)	5.7 (4.9-6.4)
HDL cholesterol, mmol/L	1.4 (1.2-1.7)	1.3 (1.1-1.6)	1.3 (1.1-1.6)	1.3 (1.1-1.6)
Systolic blood pressure, mmHg	106.7 (5.9)	125.1 (7.7)	146.2 (6.6)	167.2 (11.5)
Diastolic blood pressure, mmHg	66.7 (5.1)	77.6 (6.3)	85.5 (7.0)	91.6 (9.3)
Isolated systolic hypertension	0 (0.0%)	0 (0.0%)	208,081 (66.3%)	41,405 (40.1%)
Isolated diastolic hypertension	355 (0.2%)	14,395 (2.3%)	18,670 (6.0%)	1,004 (1.0%)
Statins	1,570 (0.8%)	21,526 (3.4%)	19,798 (6.3%)	4,010 (3.9%)
Blood pressure lowering treatments	21,643 (10.7%)	113,436 (17.8%)	139,753 (44.5%)	66,086 (64.1%)
Thiazide diuretics	746 (0.4%)	16,593 (2.6%)	42,662 (13.6%)	22,964 (22.3%)
Beta-blockers	3,443 (1.7%)	25,632 (4.0%)	36,367 (11.6%)	17,565 (17.0%)
ACEI/ARBs	1,572 (0.8%)	25,491 (4.0%)	43,784 (14.0%)	19,760 (19.2%)
Calcium-channel blockers	454 (0.2%)	11,826 (1.9%)	28,232 (9.0%)	14,419 (14.0%)
Number of baseline BP measurements	2 (1-3)	2 (1-3)	3 (1-7)	4 (1-9)

[1] Patients are classified to the highest category based on their SBP or DBP.
[2]Continuous variables are summarized as median (inter-quartile range), except for systolic and diastolic blood pressure, summarized as mean (standard deviation). Categorical variables are summarized as number (% in the corresponding blood pressure category).
[3] Patients with missing baseline blood pressure measurements (N=679,354) were excluded.
[4] Missing data (%): Smoking status, 15%; Body mass index, 56%; Total cholesterol, 80%; HDL cholesterol, 84%.
Abbreviations: ACEI, Angiotensin-converting enzyme inhibitors; ARBs, Alpha-adrenoreceptor blocking drugs; COPD, chronic obstructive pulmonary disease; HDL, high-density lipoprotein cholesterol.

Table S 3 Summary characteristics of people with recorded (main analysis dataset) and missing blood pressure among eligible patients (N=1,937,360).

	Baseline BP recorded (N=1,258,006)	Baseline BP missing (N=679,354)	P-value for difference*
Age, years	45.0 (34.9-58.9)	40.6 (32.0-52.5)	P<0.0001
Female sex	732,657 (58.2%)	238,561 (35.9%)	P<0.0001
White ethnicity	656,162 (89.8%)	254,958 (92.2%)	P<0.0001
Most deprived quintile	251,438 (20.0%)	136,206 (20.5%)	P<0.0001
Smoking status			
Ex-smoker	185,167 (17.4%)	41,728 (12.4%)	P<0.0001
Current smoker	232,808 (21.8%)	52,550 (15.6%)	P<0.0001
Medical history			
Diabetes	45,702 (3.6%)	3,064 (0.5%)	P<0.0001
Kidney disease	14,767 (1.2%)	2,728 (0.4%)	P<0.0001
COPD	22,177 (1.8%)	7,308 (1.1%)	P<0.0001
Measurements			
Body mass index, kg/m^2	25.6 (22.8-29.0)	24.9 (22.3-28.3)	P<0.0001
Total cholesterol, mmol/L	5.3 (4.6-6.1)	5.3 (4.6-6.1)	P=0.10
HDL cholesterol, mmol/L	1.3 (1.1-1.6)	1.3 (1.1-1.6)	P=0.03
Medication use			
Thiazide diuretics	82,965 (6.6%)	6,451 (1.0%)	P<0.0001
Beta-blockers	83,007 (6.6%)	9,320 (1.4%)	P<0.0001
ACEI/ARBs	90,607 (7.2%)	5,449 (0.8%)	P<0.0001
Calcium-channel blockers	54,931 (4.4%)	3,203 (0.5%)	P<0.0001
Statins	46,904 (3.7%)	1,568 (0.2%)	P<0.0001

*Two-sided, with Bonferroni correction for multiple comparisons.

Continuous variables are summarised as median (IQR) and categorical as N (%).

Abbreviations: ACEI, Angiotensin-converting enzyme inhibitors; ARBs, Alpha-adrenoreceptor blocking drugs; COPD, chronic obstructive pulmonary disease; HDL, high-density lipoprotein cholesterol.

Table S 4 Estimates of lifetime risks and life-years lost to CVD associated with hypertension at different index ages (30, 60, 80) up to age 95.

EVENTS	Lifetime risks				Life-years lost to CVD		
	Normotensives	Hypertensives	Lifetime risk difference	Lifetime risk ratio	All hypertensives	Isolated systolic hypertension	Isolated diastolic hypertension
Index age 30							
Stable angina	4.9 (4.7-5.2)	8.9 (8.7-9.2)	4.0 (3.7, 4.3)	1.82 (1.76-1.87)	1.11 (1.03,1.19)	0.3 (0.26,0.33)	0.02 (-0.01,0.04)
Unstable angina	6.7 (6.4-7.0)	10.1 (9.8-10.3)	3.4 (3.0, 3.7)	1.5 (1.46-1.55)	1.04 (0.95,1.13)	0.21 (0.17,0.25)	0.01 (-0.01,0.04)
Myocardial infarction	5.5 (5.3-5.8)	8.0 (7.8-8.3)	2.5 (2.2, 2.8)	1.45 (1.41-1.49)	0.75 (0.67,0.83)	0.21 (0.17,0.25)	0.06 (0.03,0.08)
Unheralded CHD death	1.9 (1.8-2.1)	2.5 (2.4-2.6)	0.6 (0.3, 0.8)	1.29 (1.22-1.36)	0.15 (0.11,0.2)	0.04 (0.02,0.05)	0.03 (0.01,0.05)
Heart failure	5.2 (4.9-5.6)	7.8 (7.6-8.1)	2.6 (2.2, 3.0)	1.5 (1.44-1.55)	0.58 (0.51,0.64)	0.1 (0.07,0.13)	0.04 (0.02,0.07)
Cardiac arrest/SCD	1.8 (1.7-2.0)	2.3 (2.2-2.4)	0.5 (0.3, 0.7)	1.26 (1.17-1.34)	0.16 (0.11,0.2)	0.01 (-0.01,0.03)	0.03 (0.00,0.05)
Transient ischaemic attack	5.9 (5.6-6.2)	6.5 (6.3-6.7)	0.6 (0.3, 1.0)	1.11 (1.07-1.14)	0.26 (0.18,0.33)	0.06 (0.03,0.09)	0.02 (0.00,0.05)
Ischaemic stroke	6.5 (6.2-6.9)	7.6 (7.3-7.8)	1.0 (0.7, 1.4)	1.16 (1.12-1.2)	0.35 (0.27,0.42)	0.06 (0.03,0.09)	0.00 (-0.03,0.03)
Subarachnoid haemorrhage	0.6 (0.5-0.7)	0.9 (0.7-1.0)	0.3 (0.2, 0.4)	1.48 (1.27-1.68)	0.09 (0.06,0.12)	0.04 (0.02,0.05)	0.00 (-0.01,0.01)
Intracerebral haemorrhage	0.9 (0.8-1.0)	1.3 (1.2-1.4)	0.4 (0.2, 0.5)	1.4 (1.29-1.51)	0.1 (0.07,0.14)	0.03 (0.02,0.04)	0.00 (-0.01,0.02)
Peripheral arterial disease	4.5 (4.2-4.7)	5.8 (5.6-6.0)	1.3 (1.0, 1.6)	1.3 (1.25-1.34)	0.4 (0.33,0.46)	0.14 (0.11,0.17)	-0.01 (-0.03,0.01)
Abdominal aortic aneurysm	1.5 (1.4-1.7)	1.6 (1.5-1.7)	0.1 (-0.1, 0.3)	1.05 (0.97-1.13)	0.04 (0,0.07)	-0.01 (-0.02,0)	0.01 (0.00,0.03)
Total CVD	**46.1 (45.5-46.8)**	**63.3 (62.9-63.8)**	**17.2 (13.9, 20.5)**	**1.37 (1.36-1.39)**	**5.02 (4.84,5.19)**	**1.18 (1.1,1.26)**	**0.23 (0.16,0.29)**
Index age 60							
Stable angina	4.5 (4.3-4.7)	8.1 (7.9-8.4)	3.6 (3.3, 3.9)	1.81 (1.75-1.87)	0.76 (0.71,0.81)	0.36 (0.32,0.4)	0.00 (0.00,0.00)
Unstable angina	5.9 (5.6-6.2)	8.6 (8.3-8.9)	2.7 (2.4, 3.0)	1.45 (1.41-1.5)	0.61 (0.55,0.67)	0.24 (0.19,0.28)	0.00 (0.00,0.00)
Myocardial infarction	5.0 (4.8-5.2)	7.1 (6.9-7.4)	2.1 (1.8, 2.4)	1.43 (1.38-1.48)	0.46 (0.41,0.52)	0.24 (0.2,0.28)	0.01 (0.00,0.01)
Unheralded CHD death	1.9 (1.8-2.1)	2.4 (2.3-2.6)	0.5 (0.3, 0.7)	1.25 (1.18-1.32)	0.11 (0.07,0.14)	0.05 (0.03,0.08)	0.00 (0.00,0.01)
Heart failure	5.5 (5.2-5.9)	8.0 (7.7-8.3)	2.5 (2.1, 2.9)	1.45 (1.39-1.5)	0.47 (0.41,0.53)	0.17 (0.13,0.21)	0.01 (0.00,0.01)
Cardiac arrest/SCD	1.7 (1.6-1.9)	2.0 (1.9-2.2)	0.3 (0.1, 0.5)	1.16 (1.08-1.24)	0.08 (0.05,0.11)	0.01 (-0.01,0.04)	0.00 (0.00,0.00)
Transient ischaemic attack	5.9 (5.6-6.3)	6.6 (6.4-6.8)	0.6 (0.3, 1.0)	1.11 (1.07-1.15)	0.2 (0.13,0.26)	0.08 (0.04,0.13)	0.00 (0.00,0.00)
Ischaemic stroke	6.6 (6.3-7.0)	7.7 (7.5-8.0)	1.1 (0.7, 1.5)	1.16 (1.12-1.21)	0.27 (0.21,0.34)	0.1 (0.05,0.14)	0.00 (0.00,0.00)
Subarachnoid haemorrhage	0.5 (0.4-0.6)	0.7 (0.6-0.9)	0.3 (0.1, 0.4)	1.52 (1.27-1.77)	0.05 (0.03,0.07)	0.03 (0.02,0.05)	0.00 (0.00,0.00)
Intracerebral haemorrhage	0.9 (0.8-1.0)	1.3 (1.2-1.4)	0.4 (0.2, 0.5)	1.41 (1.3-1.53)	0.08 (0.05,0.1)	0.04 (0.02,0.06)	0.00 (0.00,0.00)
Peripheral arterial disease	4.4 (4.1-4.6)	5.9 (5.7-6.1)	1.5 (1.2, 1.8)	1.35 (1.3-1.4)	0.34 (0.29,0.39)	0.19 (0.15,0.23)	0.00 (0.00,0.00)
Abdominal aortic aneurysm	1.7 (1.5-1.9)	1.7 (1.5-1.8)	0.0 (-0.2, 0.2)	0.99 (0.92-1.06)	0.02 (-0.02,0.05)	-0.01 (-0.04,0.01)	0.00 (0.00,0.00)
Total CVD	**44.6 (43.9-45.3)**	**60.2 (59.6-60.7)**	**15.6 (12.4-18.8)**	**1.35 (1.33-1.37)**	**3.44 (3.3,3.58)**	**1.5 (1.4,1.61)**	**0.03 (0.02,0.03)**
Index age 80							
Stable angina	3.6 (3.4-3.8)	6.6 (6.3-6.8)	3 (2.7, 3.2)	1.84 (1.77-1.9)	0.31 (0.28,0.33)	0.16 (0.14,0.18)	0.00 (0.00,0.00)
Unstable angina	4.7 (4.5-5.0)	6.9 (6.6-7.2)	2.2 (1.9, 2.5)	1.46 (1.4-1.53)	0.23 (0.2,0.26)	0.1 (0.08,0.12)	0.00 (0.00,0.00)
Myocardial infarction	4.0 (3.8-4.2)	5.9 (5.6-6.1)	1.8 (1.6, 2.1)	1.45 (1.4-1.51)	0.19 (0.17,0.22)	0.11 (0.09,0.13)	0.00 (0.00,0.00)
Unheralded CHD death	1.8 (1.6-2.0)	2.3 (2.1-2.5)	0.5 (0.4, 0.7)	1.31 (1.21-1.41)	0.06 (0.05,0.08)	0.03 (0.02,0.05)	0.00 (0.00,0.00)
Heart failure	5.3 (4.9-5.7)	8.0 (7.6-8.4)	2.8 (2.4, 3.2)	1.53 (1.44-1.61)	0.31 (0.27,0.34)	0.12 (0.09,0.15)	0.00 (0.00,0.00)
Cardiac arrest/SCD	1.4 (1.2-1.5)	1.6 (1.5-1.7)	0.2 (0.1, 0.4)	1.17 (1.08-1.25)	0.03 (0.02,0.04)	0.01 (0,0.02)	0.00 (0.00,0.00)
Transient ischaemic attack	4.8 (4.5-5.1)	5.5 (5.3-5.7)	0.7 (0.4, 1.0)	1.14 (1.09-1.19)	0.09 (0.06,0.12)	0.04 (0.02,0.06)	0.00 (0.00,0.00)
Ischaemic stroke	5.8 (5.5-6.2)	7.1 (6.8-7.4)	1.3 (0.9, 1.6)	1.22 (1.16-1.27)	0.16 (0.12,0.19)	0.06 (0.04,0.09)	0.00 (0.00,0.00)
Subarachnoid haemorrhage	0.4 (0.4-0.5)	0.7 (0.6-0.8)	0.2 (0.1, 0.3)	1.6 (1.34-1.85)	0.03 (0.02,0.04)	0.02 (0.01,0.03)	0.00 (0.00,0.00)
Intracerebral haemorrhage	0.7 (0.6-0.8)	1.1 (1.0-1.2)	0.3 (0.2, 0.5)	1.46 (1.31-1.61)	0.04 (0.02,0.05)	0.02 (0.01,0.03)	0.00 (0.00,0.00)
Peripheral arterial disease	3.4 (3.2-3.6)	4.6 (4.4-4.8)	1.3 (1.0, 1.5)	1.38 (1.32-1.44)	0.14 (0.12,0.16)	0.08 (0.07,0.1)	0.00 (0.00,0.00)
Abdominal aortic aneurysm	1.4 (1.2-1.6)	1.5 (1.3-1.6)	0.0 (-0.1, 0.2)	1.03 (0.93-1.12)	0.01 (-0.01,0.03)	-0.01 (-0.02,0.01)	0.00 (0.00,0.00)
Total CVD	**37.3 (36.6-38.0)**	**51.7 (51.1-52.4)**	**14.4 (11.6-17.2)**	**1.39 (1.36-1.41)**	**1.59 (1.52,1.66)**	**0.75 (0.69,0.8)**	**0.00 (0.00,0.00)**

Table S 5 Hazard ratios (95% CIs) for 10 mmHg higher systolic blood pressure adjusted for age and sex.

Event	HR	Lower 95% CI	Upper 95% CI
Stable angina	1.19	1.18	1.20
Unstable angina	1.13	1.11	1.15
Myocardial infarction	1.15	1.14	1.16
Unheralded CHD death	1.12	1.10	1.15
Heart failure	1.12	1.11	1.14
Cardiac arrest/SCD	1.10	1.07	1.12
Transient ischaemic attack	1.07	1.06	1.08
Ischaemic stroke	1.16	1.14	1.18
Intracerebral haemorrhage	1.20	1.17	1.23
Subarachnoid haemorrhage	1.18	1.13	1.23
Peripheral arterial disease	1.16	1.15	1.18
Abdominal aortic aneurysm	1.02	1.00	1.05

Figure S 1 Study flow diagram

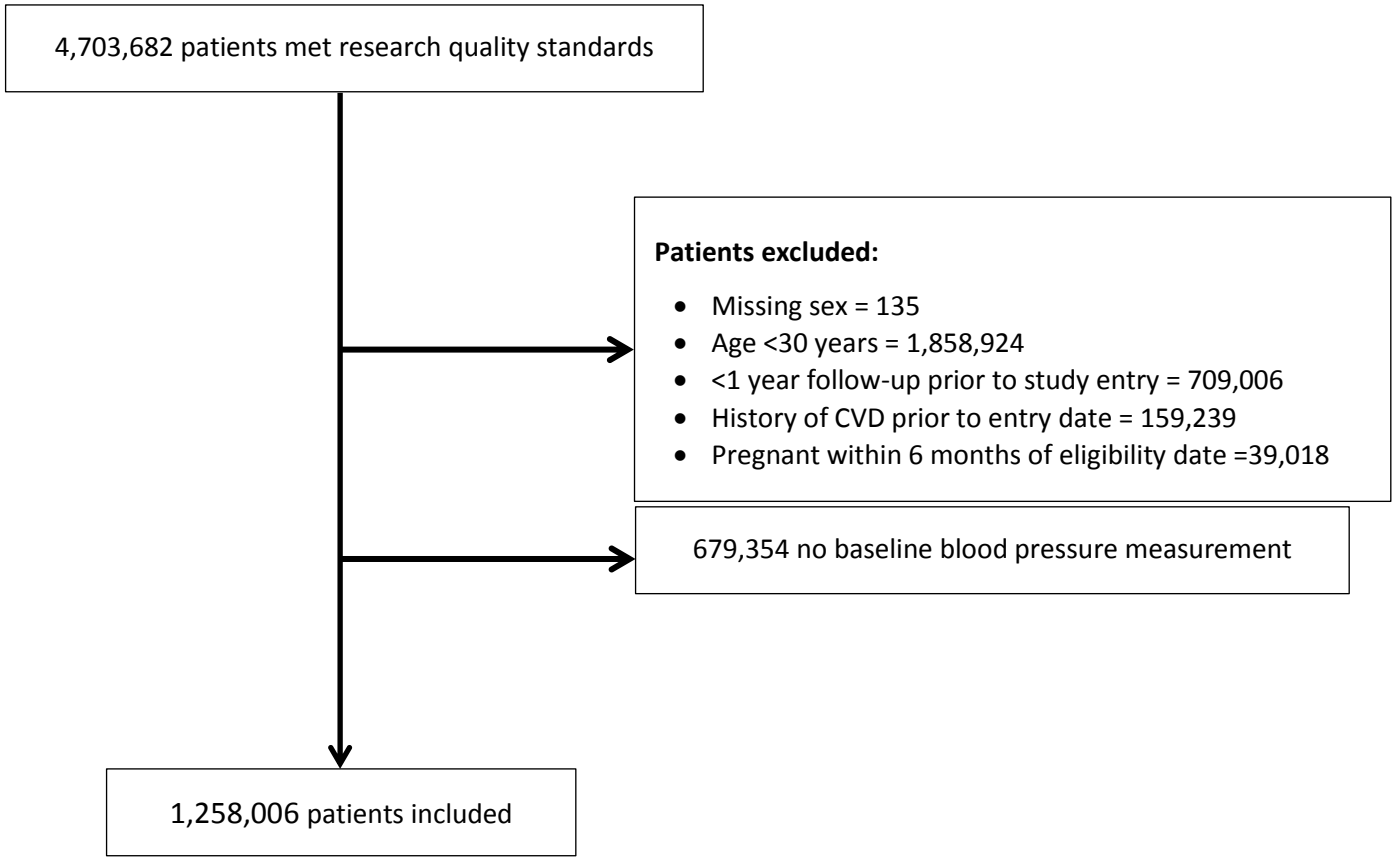


Figure S 2 The distribution of demographic characteristics among primary care practices contributing to the main analysis.

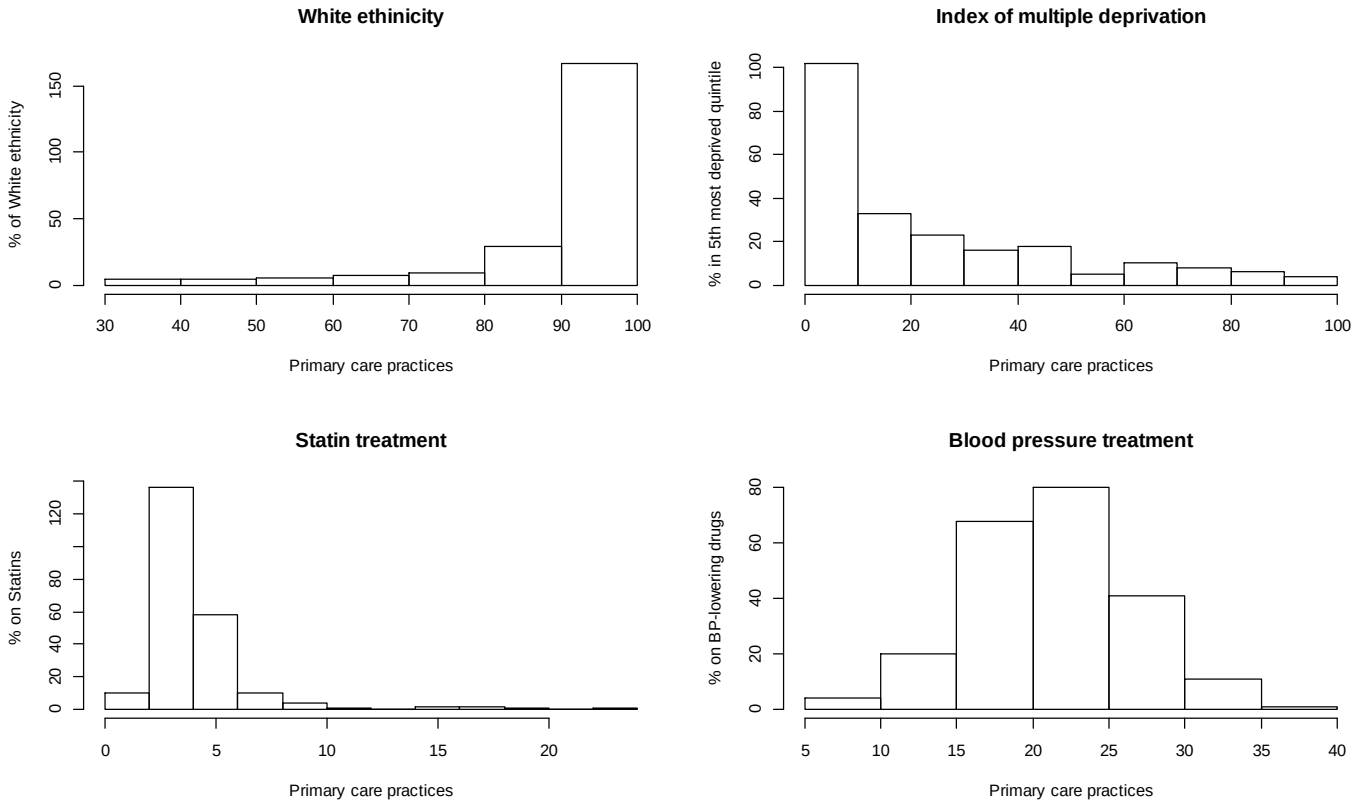
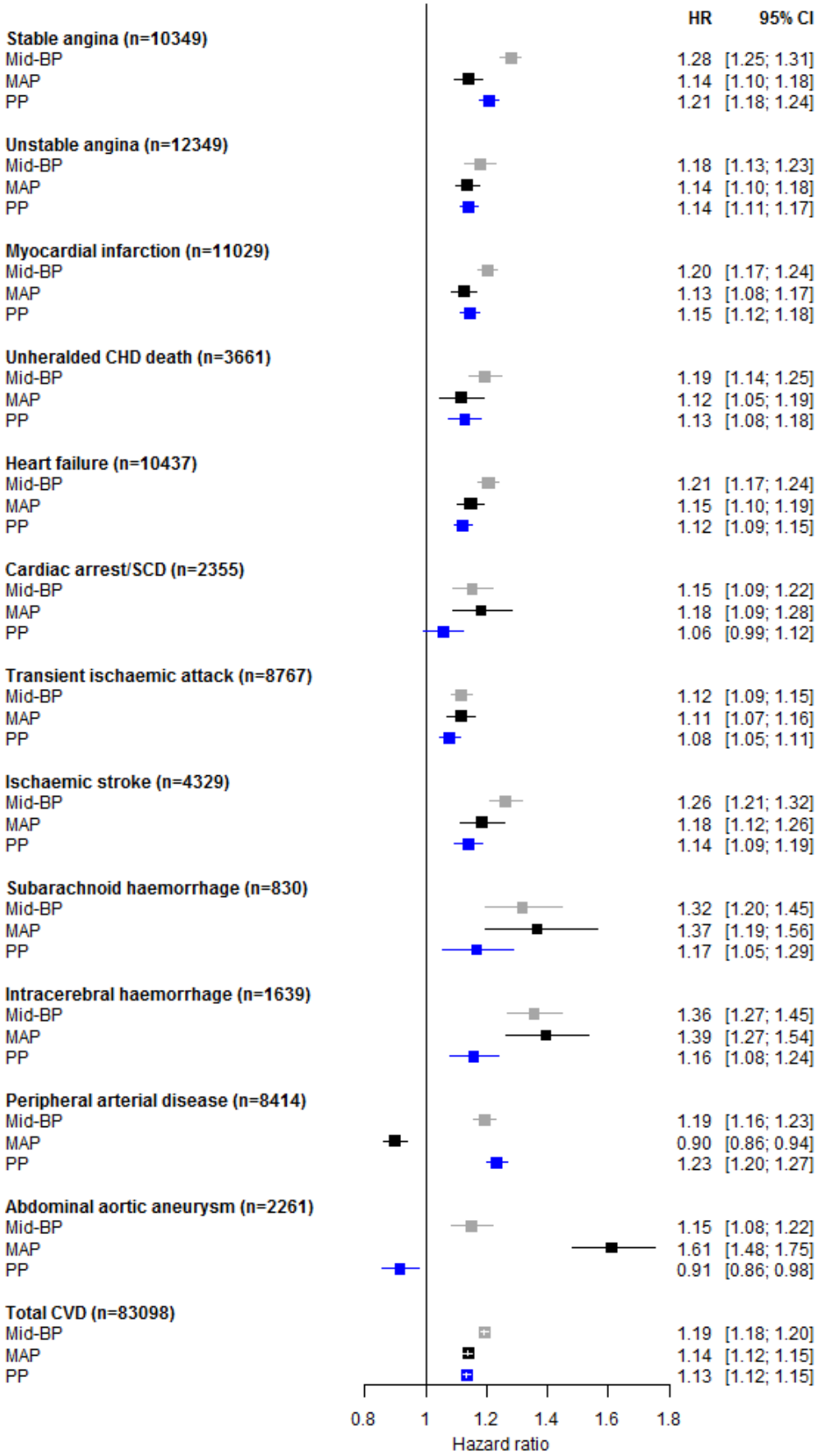
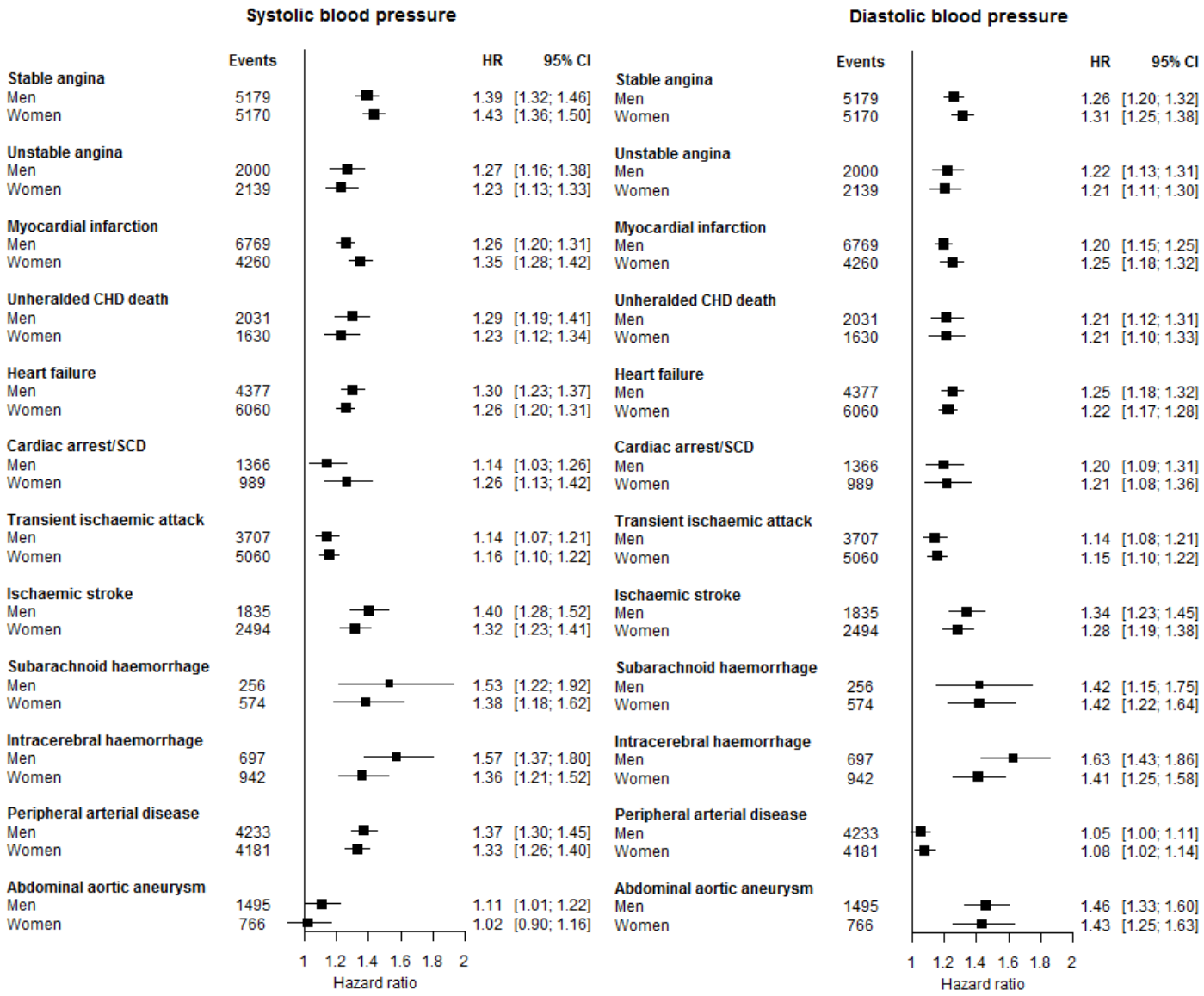


Figure S 3 Hazard ratios (95% CIs) per 10 mmHg higher mid blood pressure (mid-BP), mean arterial blood pressure (MAP) and pulse pressure (PP) adjusted for age and sex.*



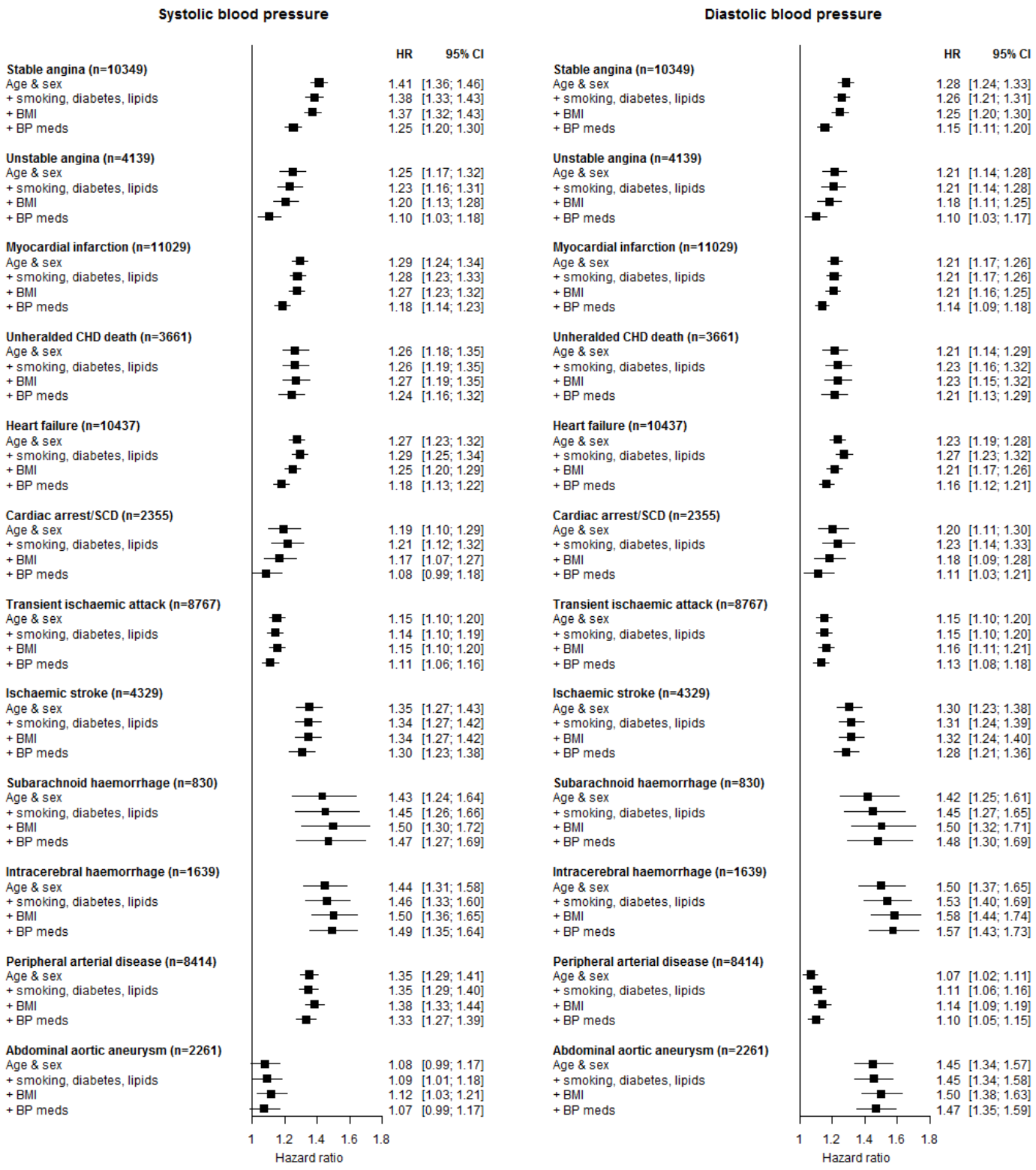
*Adjustments include age, quadratic age, and stratification by sex and primary care practice. Confidence intervals are Bonferroni-corrected (3 variables X 12 endpoints = 36 tests in total).

Figure S 4 Hazard ratios (95% CIs) by sex per 20/10 mmHg higher systolic or diastolic blood pressure adjusted for age.*



*Models were fitted separately for men and women and included continuous age, quadratic age, with stratification by primary care practice. Confidence intervals are Bonferroni-corrected (2 sexes X 12 endpoints=24 tests).

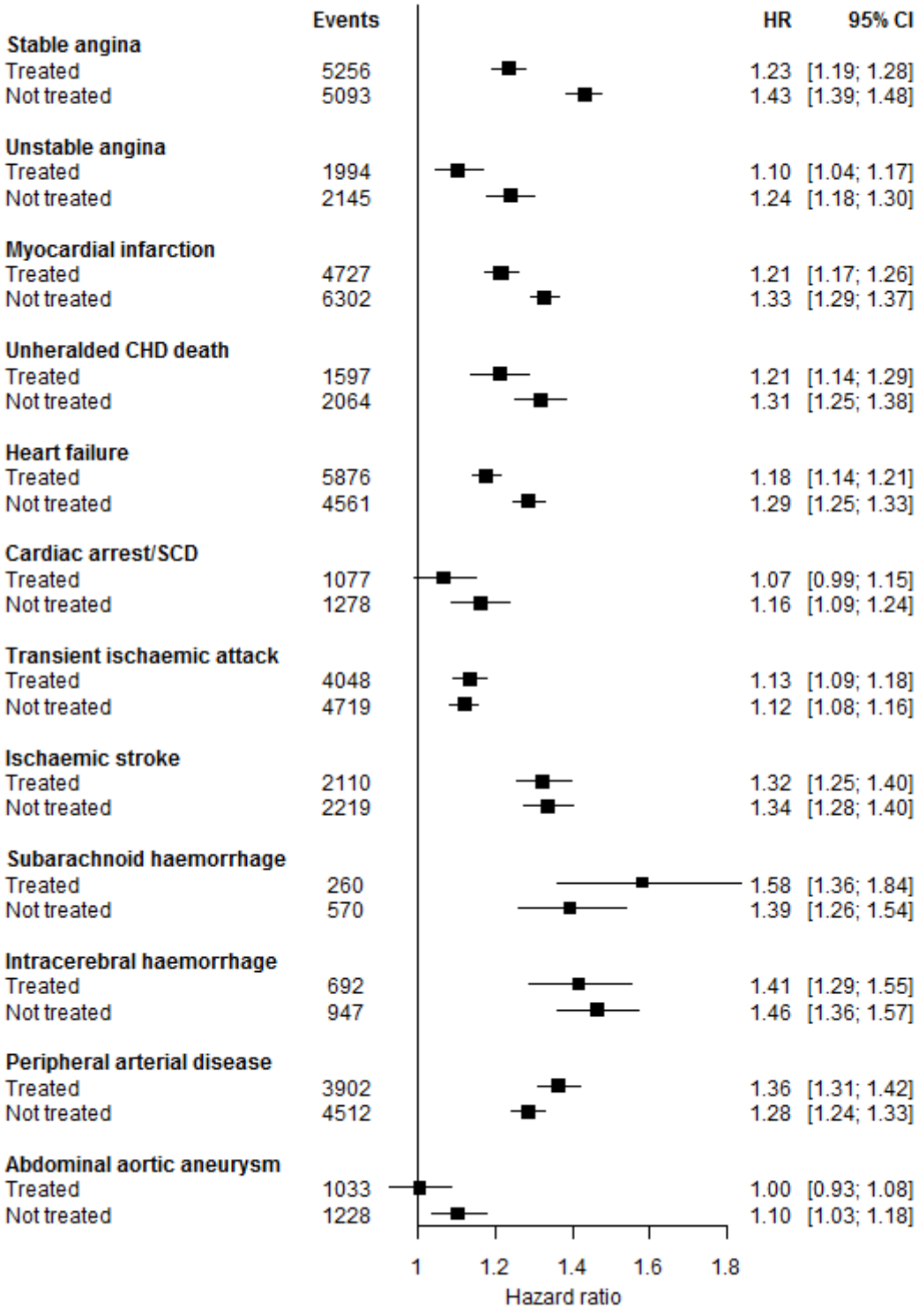
Figure S 5 Adjusted hazard ratios (95% CIs) per 20/10 mmHg higher systolic or diastolic blood pressure.*



Abbreviations: BP meds, blood pressure lowering medications; lipids include total and HDL cholesterol.

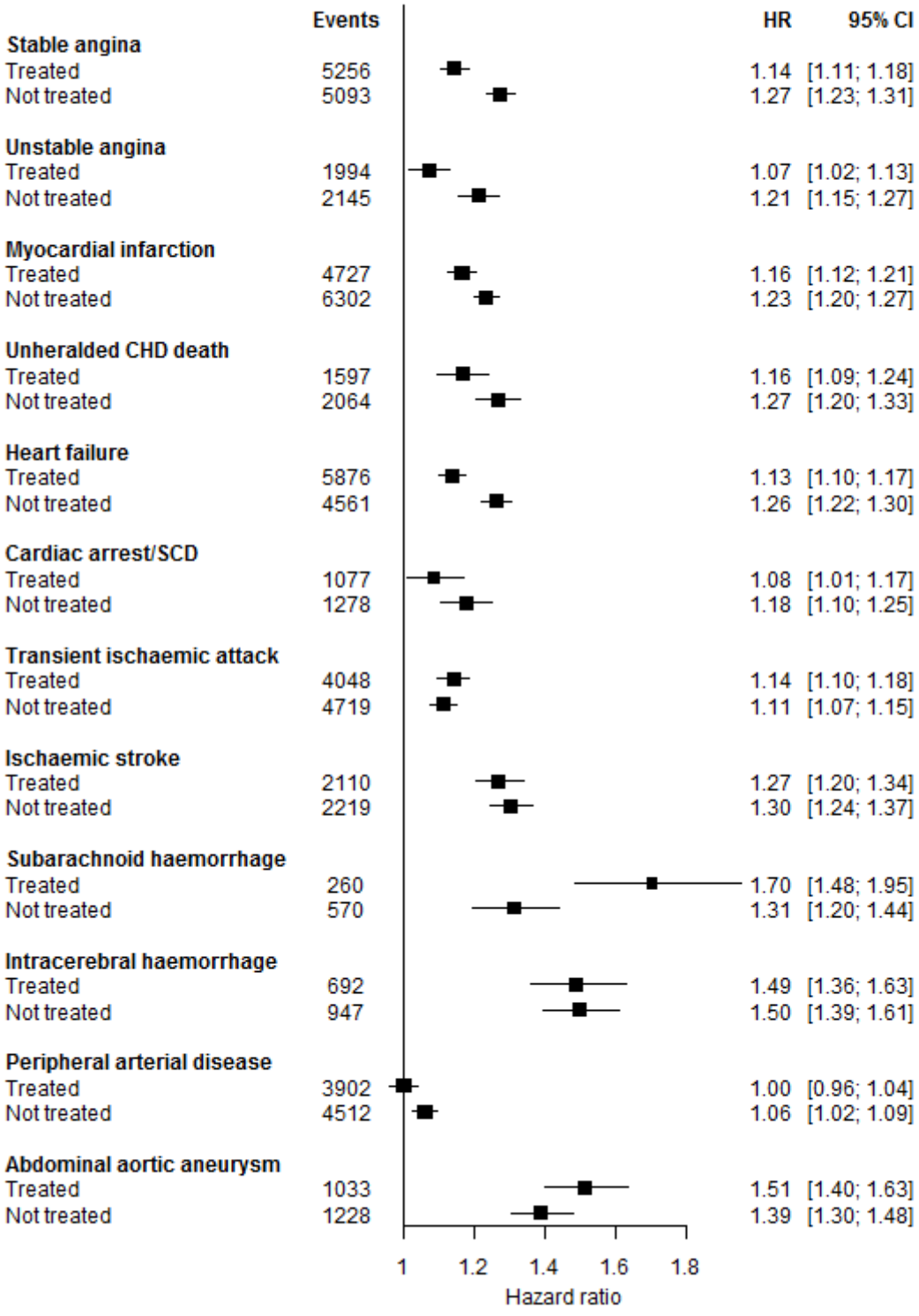
*All models included continuous age, quadratic age, with stratification by sex and primary care practice, in addition to the covariates listed above. Confidence intervals are Bonferroni-corrected (4 models X 12 endpoints=48 tests).

Figure S 6 Hazard ratios (95% CIs) per 20 mmHg higher systolic blood pressure adjusted for age and sex estimated separately in people with (N= 265,473) or without (N= 992,533) BP-lowering drugs at baseline.*



*Models were fitted separately in people treated or not treated with BP medications at baseline, with adjustments for age, quadratic age, and stratification by sex and primary care practice. Confidence intervals are Bonferroni-corrected (2 groups X 12 endpoints=24 tests in total).

Figure S 7 Hazard ratios (95% CIs) per 10 mmHg higher diastolic blood pressure adjusted for age and sex estimated separately in people with (N= 265,473) or without (N= 992,533) BP-lowering drugs at baseline.



*Models were fitted separately in people treated or not treated with BP medications at baseline, with adjustments for age, quadratic age, and stratification by sex and primary care practice. Confidence intervals are Bonferroni-corrected (2 groups X 12 endpoints=24 tests in total).

Figure S 8 Hazard ratios (95% CIs) for the associations of different cutoffs of systolic blood pressure (reference 115 mmHg) with cardiovascular endpoints in men adjusted for age (BP was modelled as a continuous variable using splines with 3 knots).

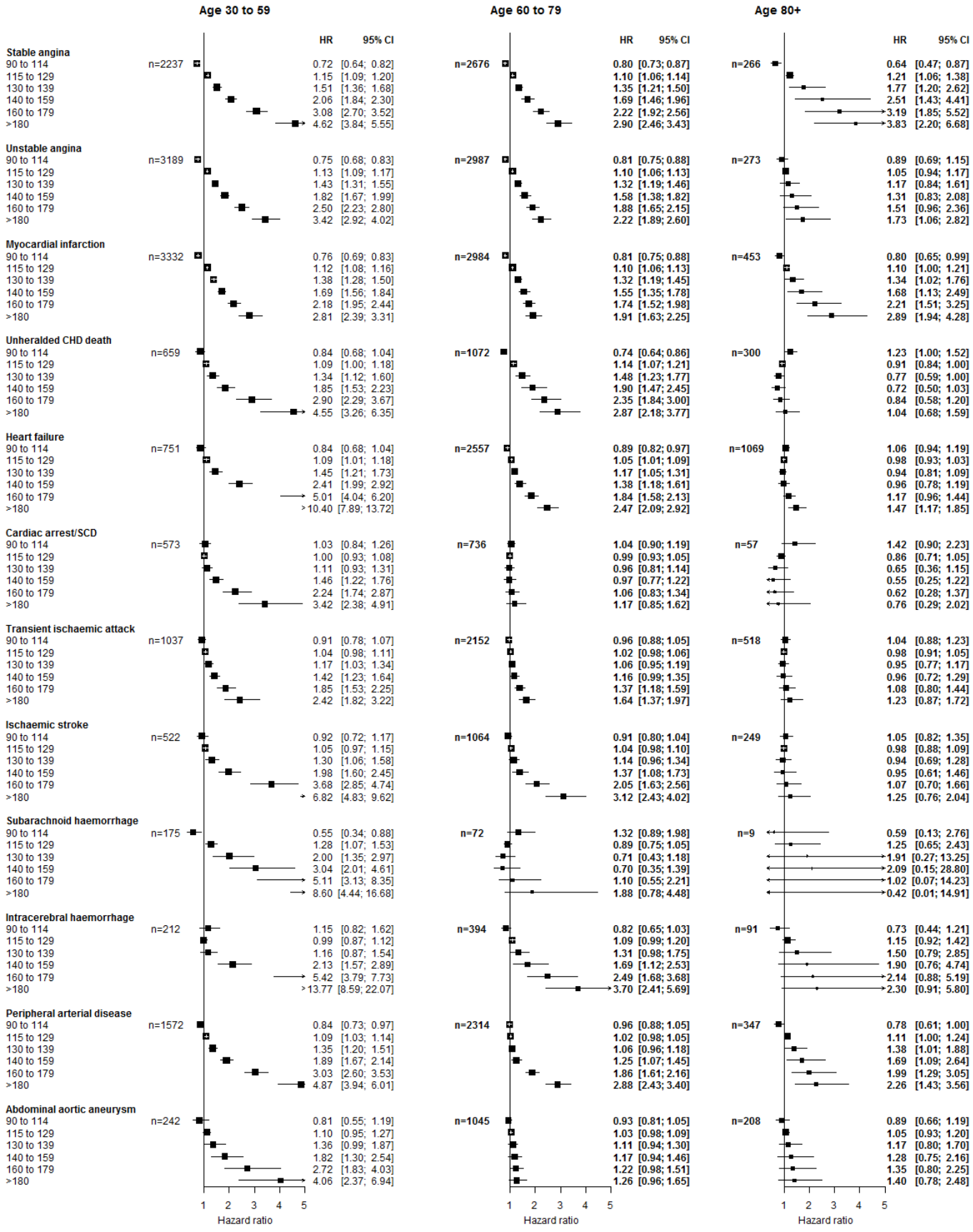


Figure S 9 Hazard ratios (95% CIs) for the associations of different cutoffs of diastolic blood pressure (reference 75 mmHg) with cardiovascular endpoints in men adjusted for age (BP was modelled as a continuous variable using splines with 3 knots).

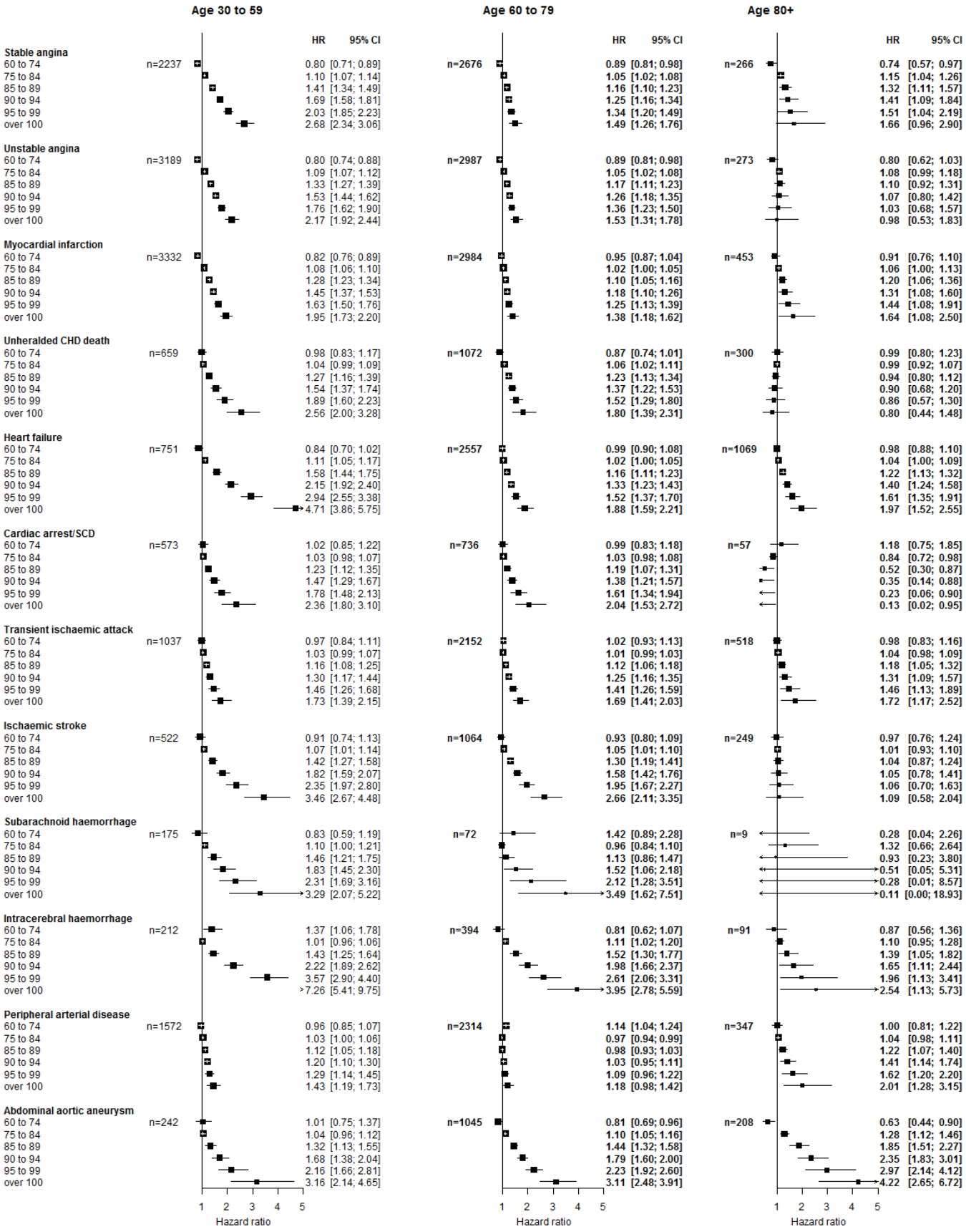


Figure S 10 Hazard ratios (95% CIs) for the associations of different cutoffs of systolic blood pressure (reference 115 mmHg) with cardiovascular endpoints in women adjusted for age (BP was modelled as a continuous variable using splines with 3 knots).

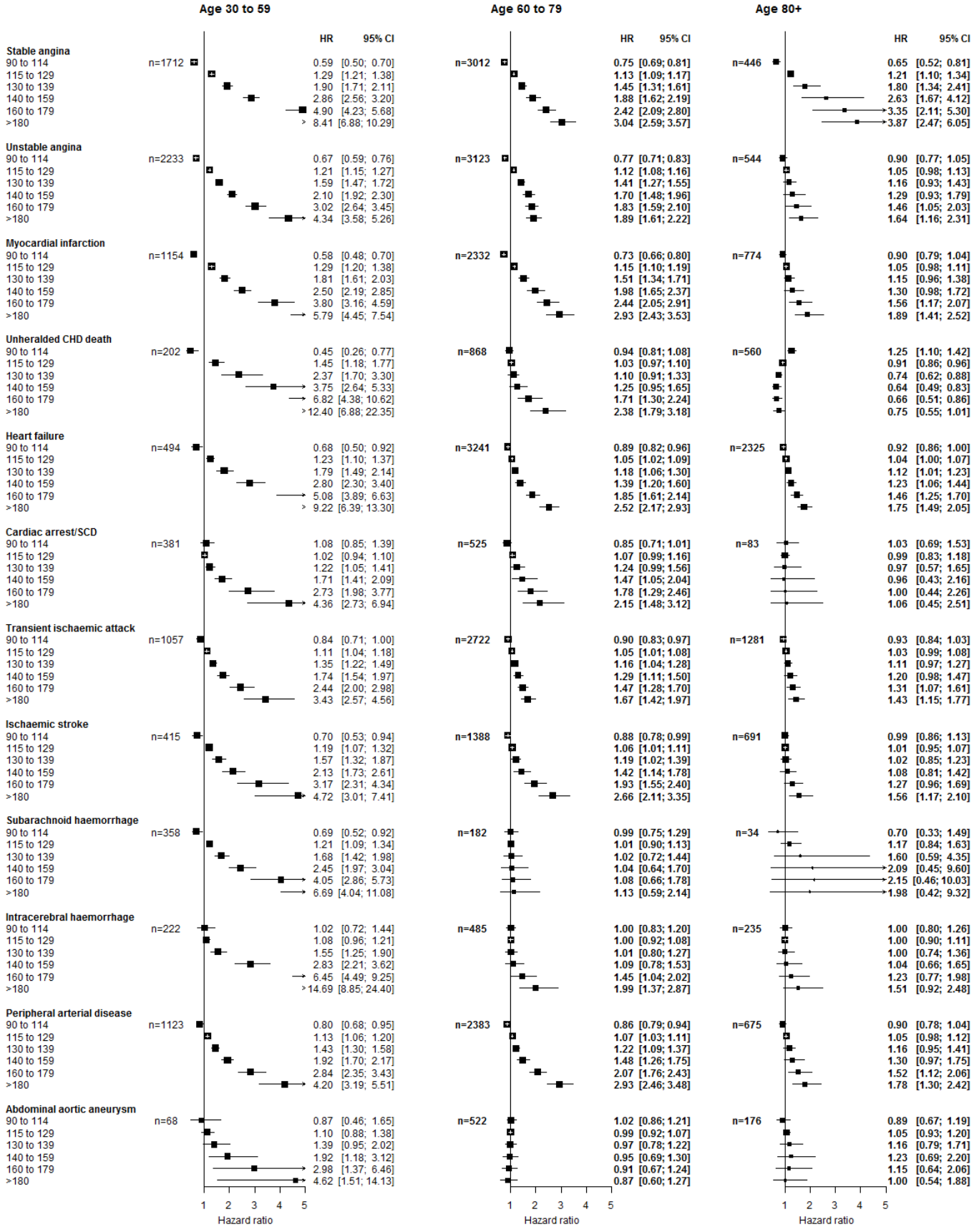


Figure S 11 Hazard ratios (95% CIs) for the associations of different cutoffs of diastolic blood pressure (reference 75 mmHg) with cardiovascular endpoints in women adjusted for age (BP was modelled as a continuous variable using splines with 3 knots).

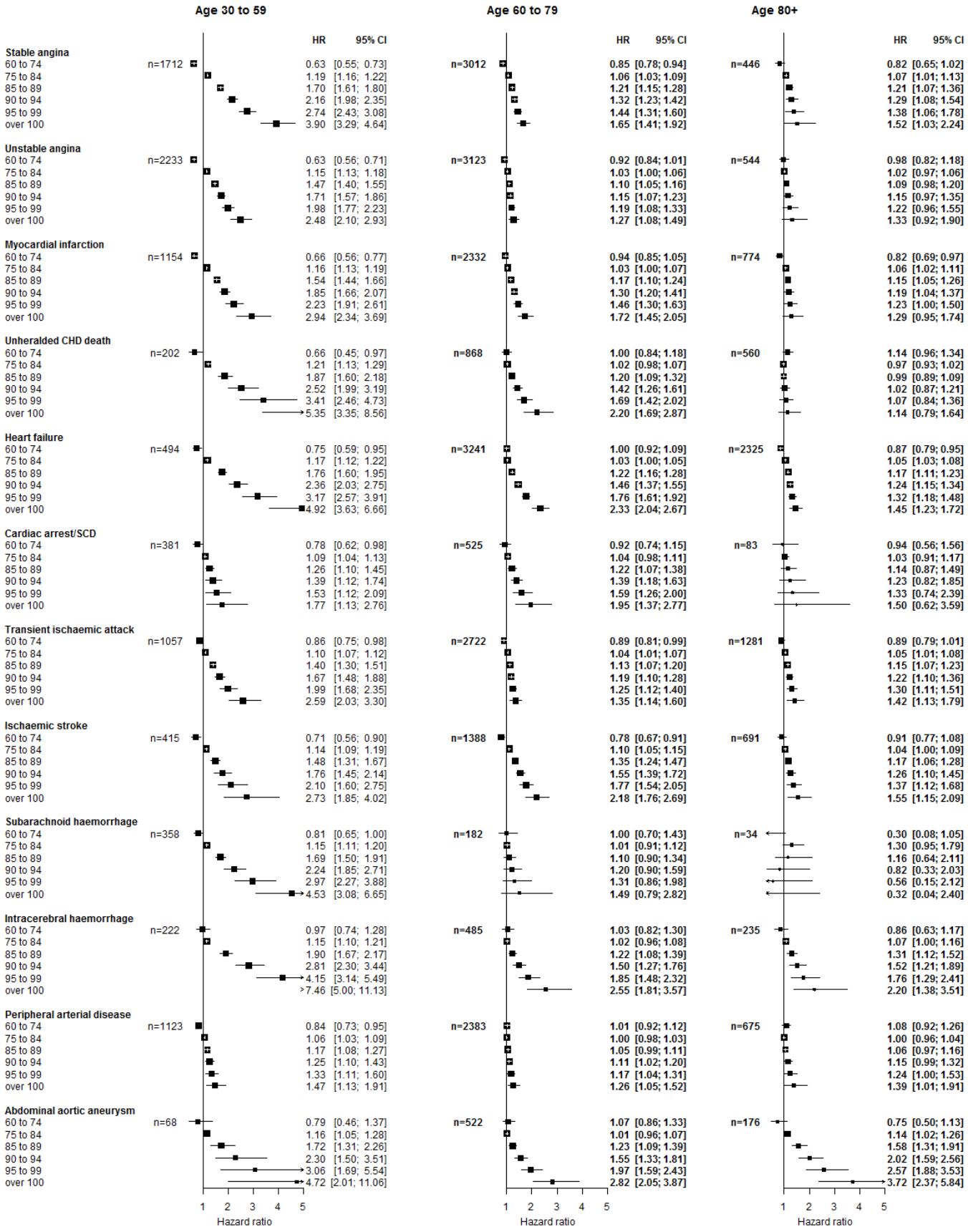


Figure S 12 Hazard ratios (95% CIs) for the associations of different cutoffs of systolic blood pressure (reference 115 mmHg) with cardiovascular endpoints in people not receiving blood pressure medications at baseline adjusted for age (BP was modelled as a continuous variable using splines with 3 knots).

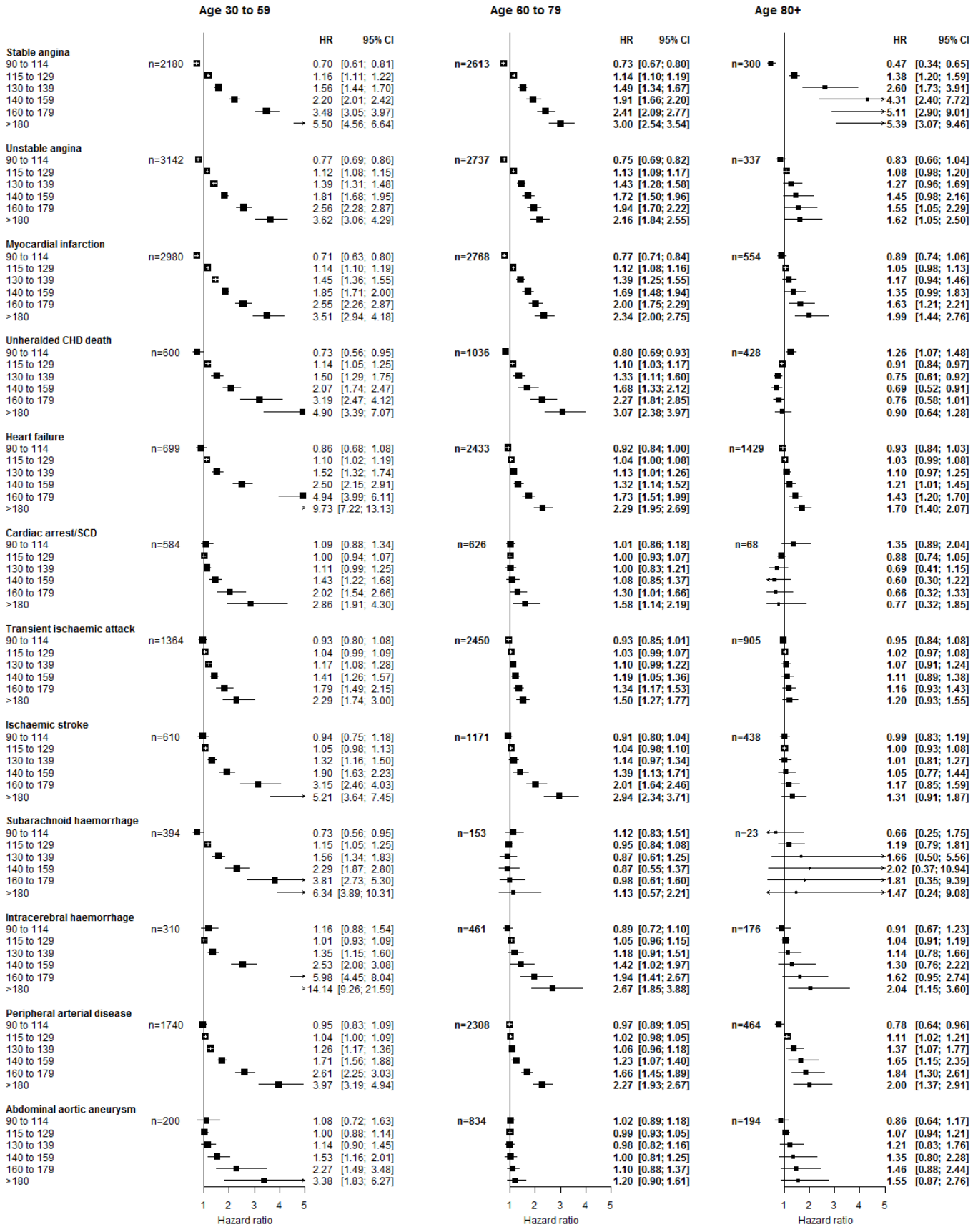


Figure S 13 Hazard ratios (95% CIs) for the associations of different cutoffs of diastolic blood pressure (reference 75 mmHg) with cardiovascular endpoints in people not receiving blood pressure medications at baseline adjusted for age (BP was modelled as a continuous variable using splines with 3 knots).

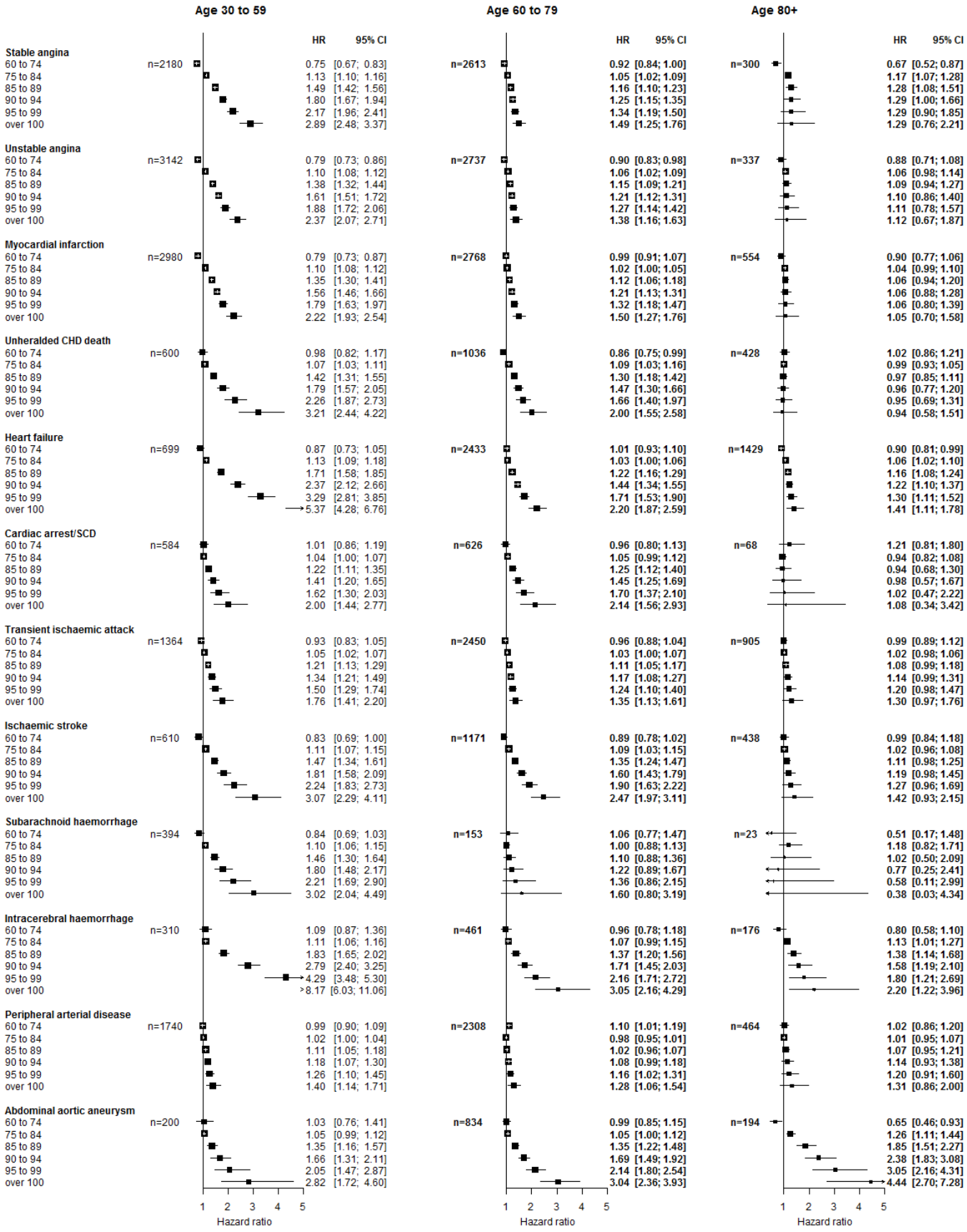


Figure S 14 Hazard ratios (95% CIs) for the associations of different cutoffs of diastolic blood pressure (reference 75 mmHg) with cardiovascular endpoints in people receiving blood pressure medications at baseline adjusted for age (BP was modelled as a continuous variable using splines with 3 knots).

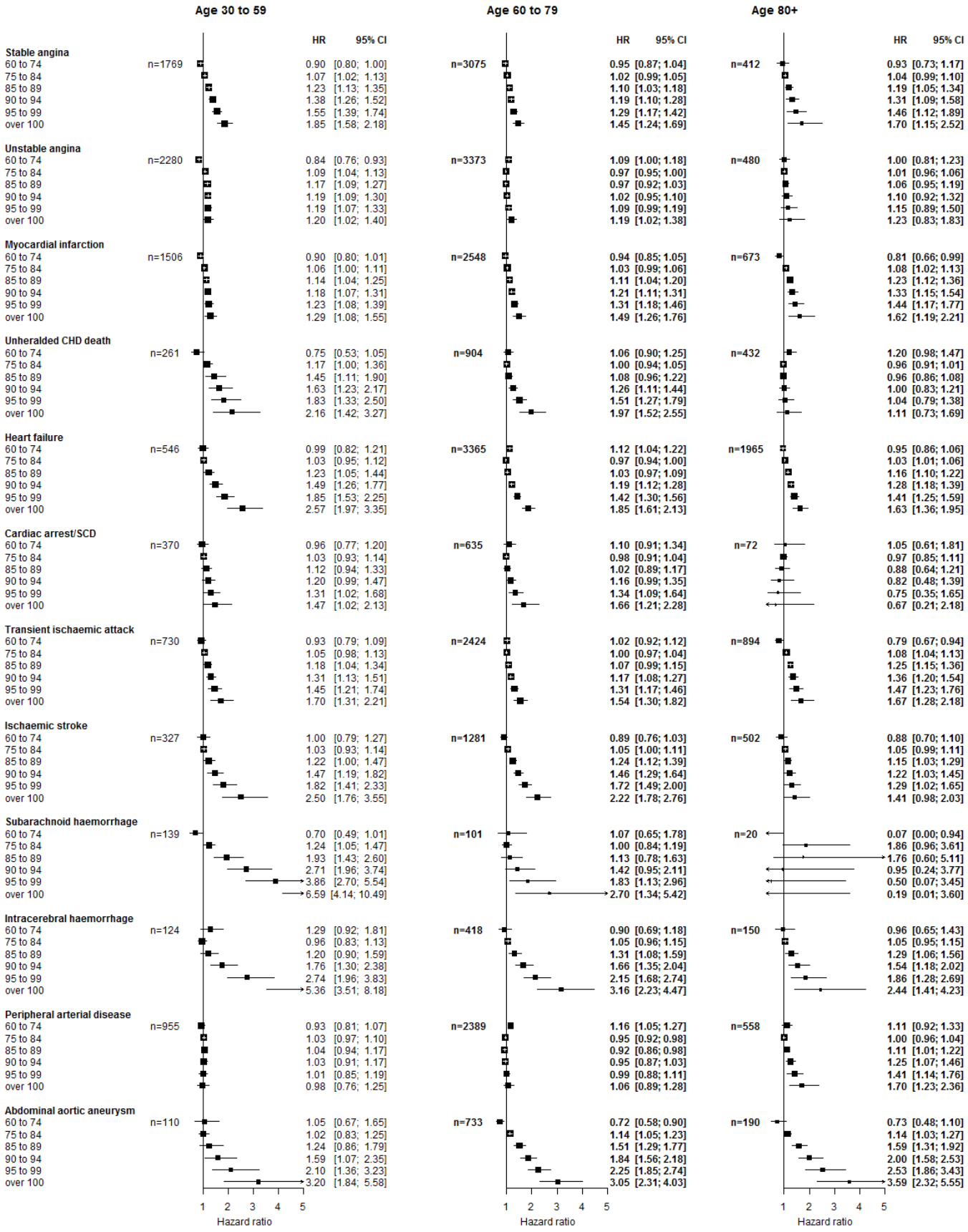


Figure S 15 Hazard ratios (95% CIs) for the associations of different cutoffs of systolic blood pressure (reference 115 mmHg) with cardiovascular endpoints in people receiving blood pressure medications at baseline adjusted for age (BP was modelled as a continuous variable using splines with 3 knots).

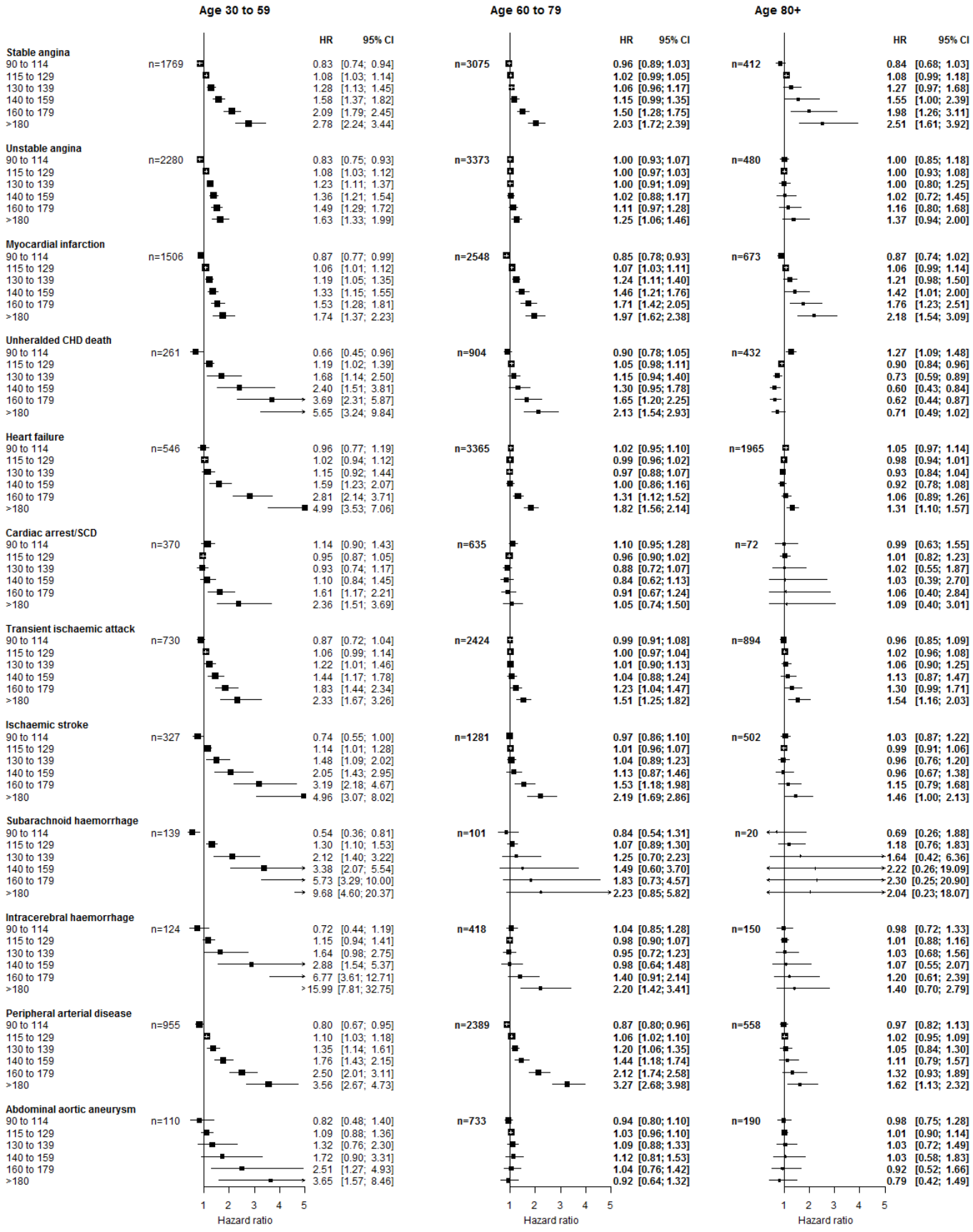
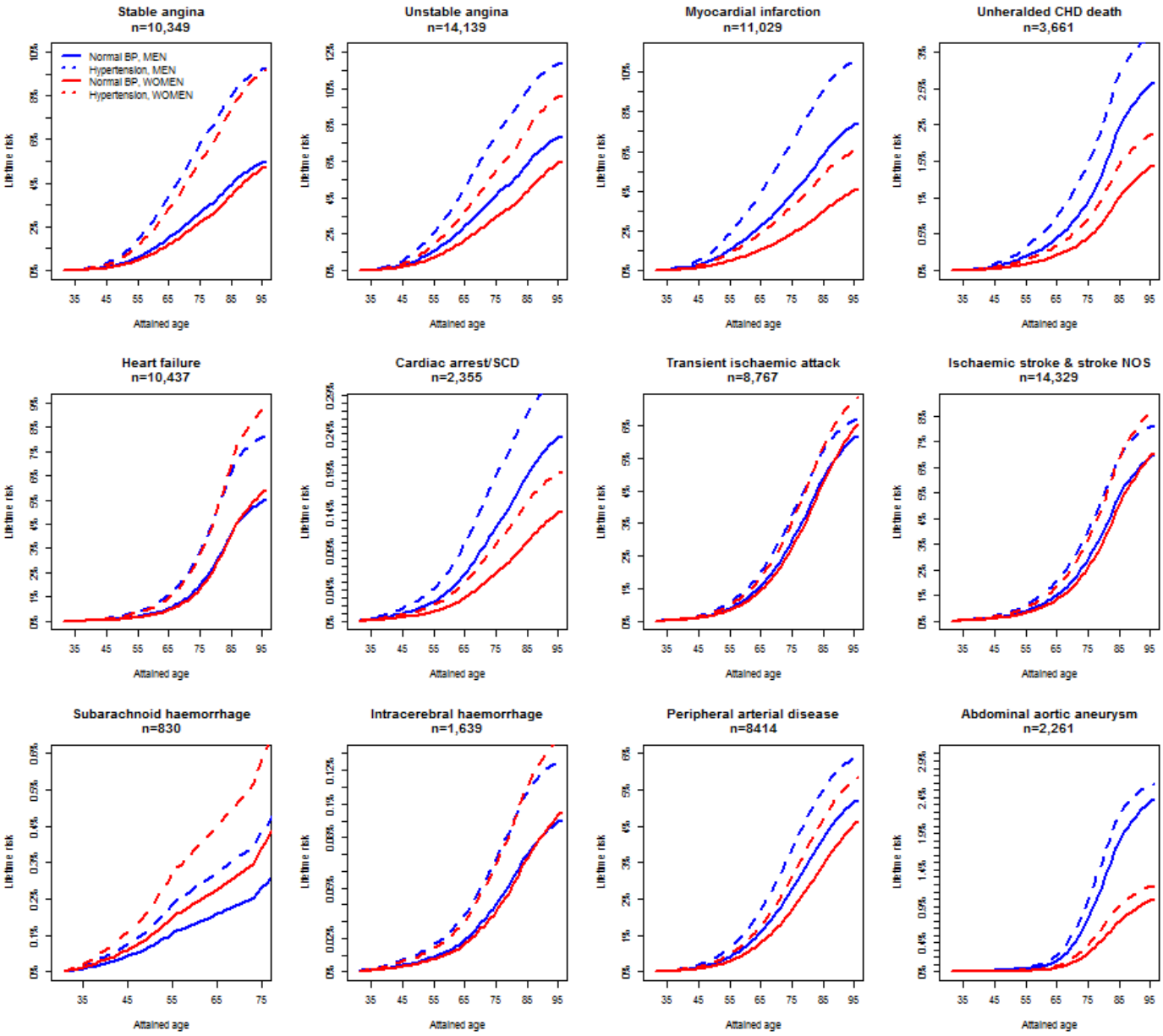
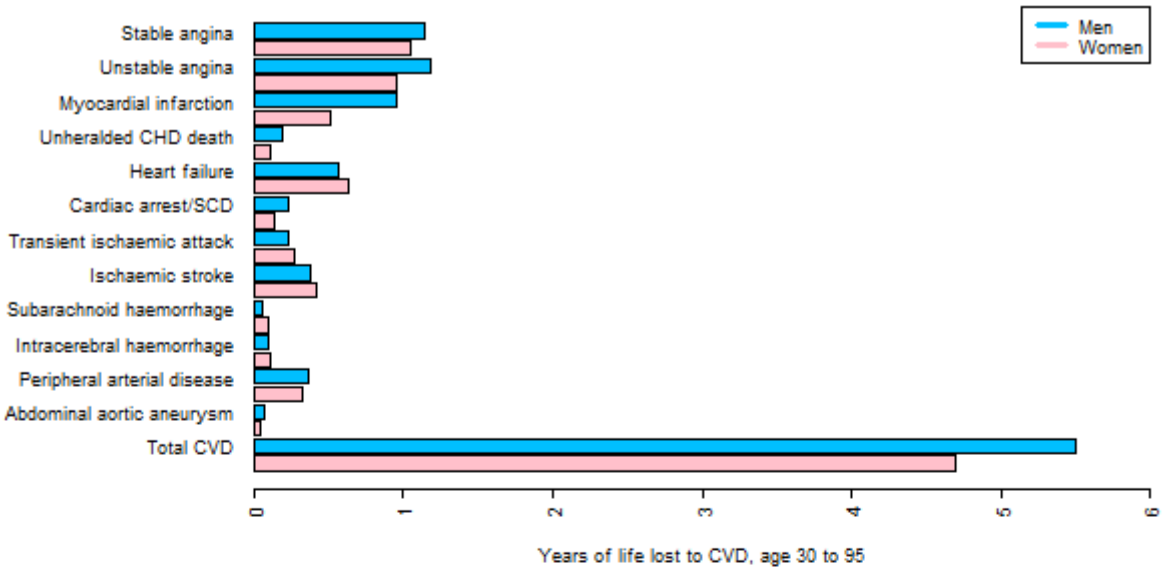


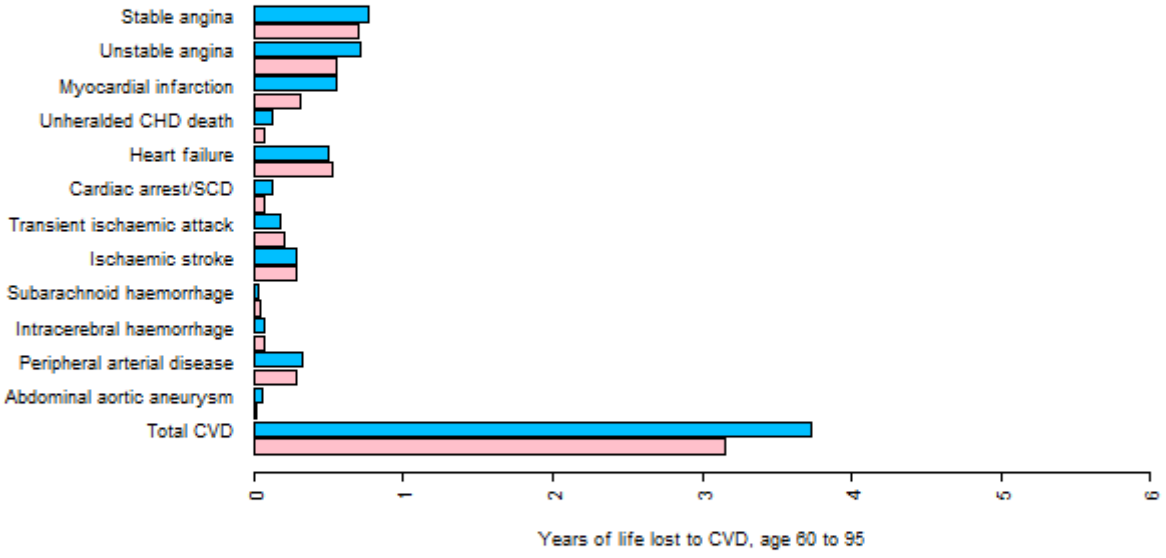
Figure S 16 Lifetime risk of 12 different cardiovascular diseases in men and women with normal blood pressure or hypertension* at index age 30.

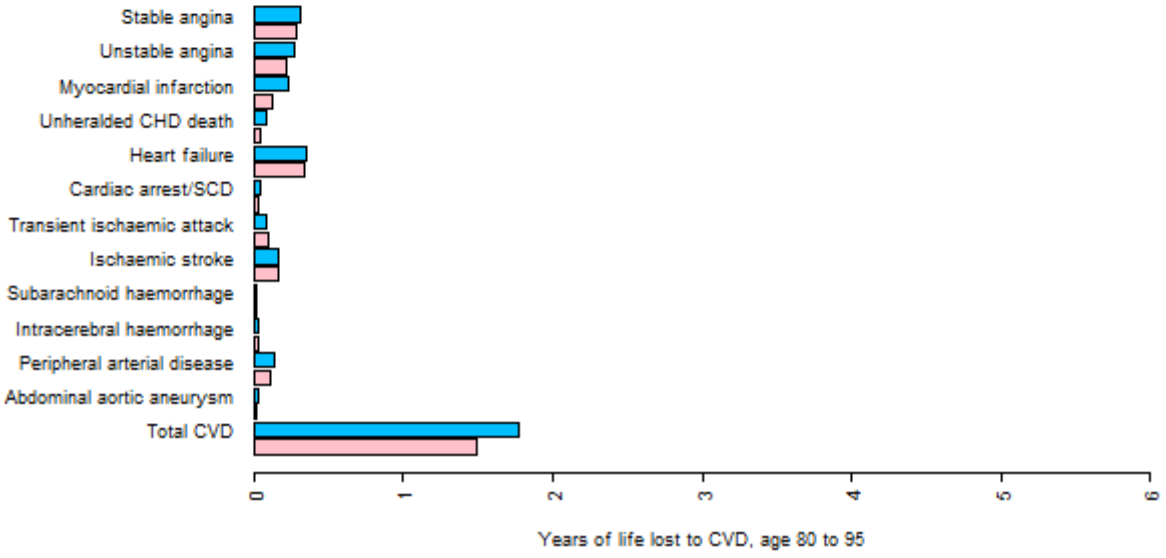


*hypertension defined as systolic blood pressure ≥140 or diastolic blood pressure ≥ 90 mmHg or use of blood pressure lowering treatments or physician-recorded diagnosis at baseline.

Figure S 17 Years of life lost to cardiovascular disease up to age 95 years in men and women associated with hypertension at index age 30, 60 and 80, adjusted for sex, smoking, diabetes, and total and HDL cholesterol.

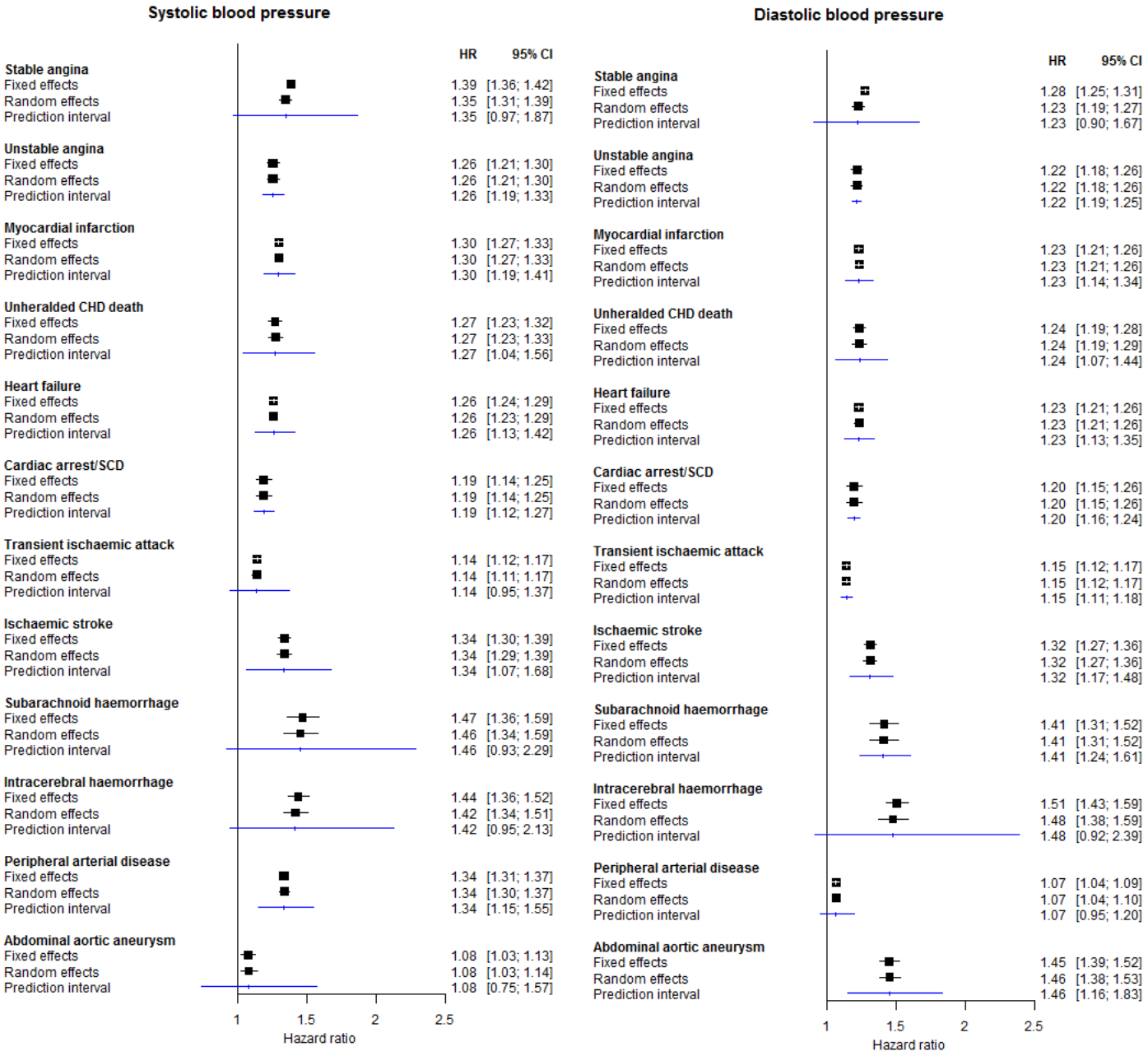






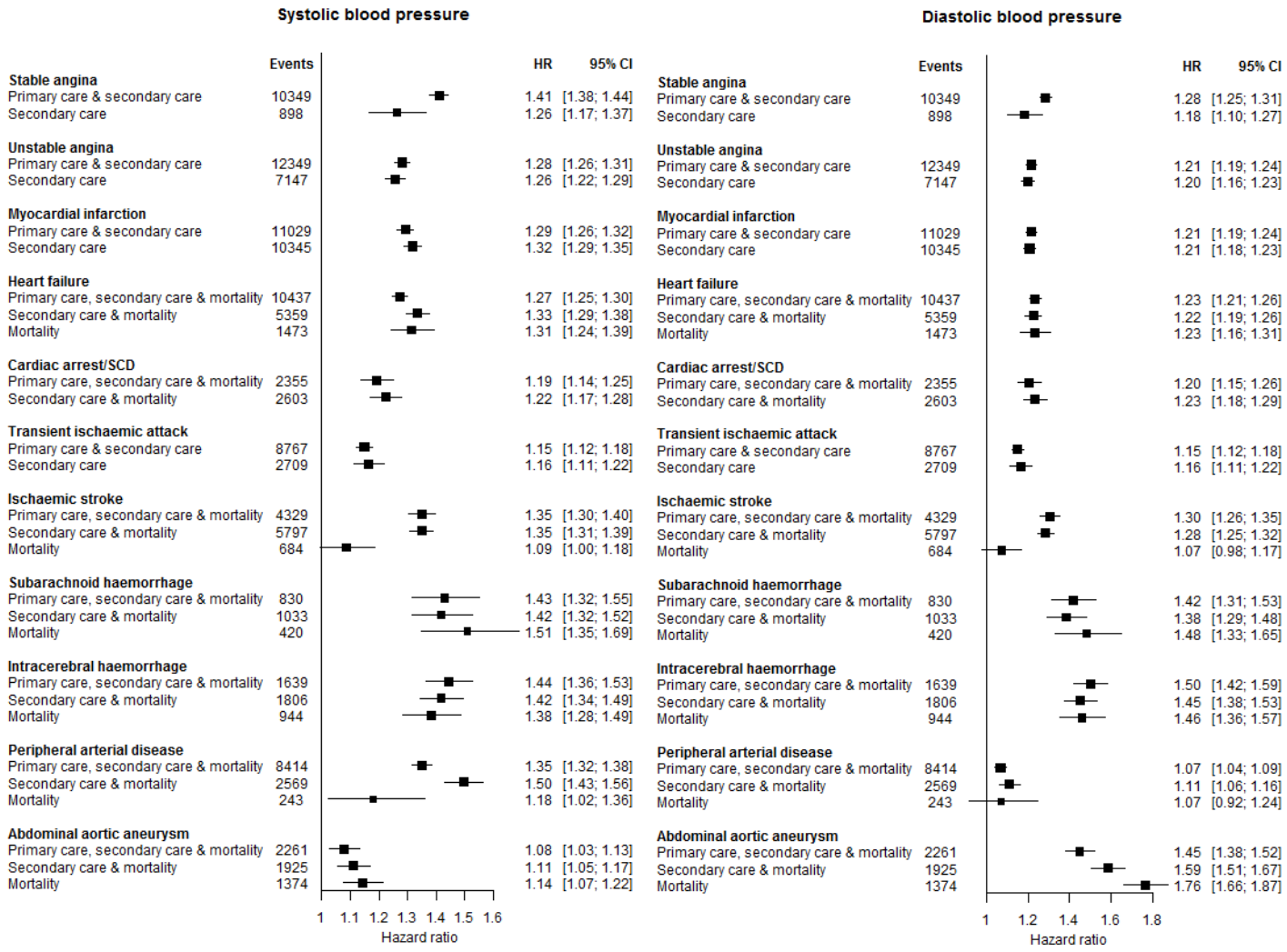
Results from sensitivity analyses

Figure S 18 Evaluation of heterogeneity* at practice level of the associations of different cardiovascular outcomes with 20/10 mmHg increase in systolic/diastolic blood pressure.



*Estimates of fixed effects are equivalent to those reported in the main analysis (but differ slightly because unlike in the main analysis were practices with at least 1 event contributed to the estimates, here we have considered studies with 2 or more for modelling purposes). Estimates of random effects account for practice level heterogeneity; differences between fixed effects and random effects signify that the heterogeneity impacts on the overall assocaitions. The prediction interval expresses uncertainty about the association in a randomly chosen practice.[1]

Figure S 19 Hazard ratios (95% CIs) per 20/10 mmHg higher systolic or diastolic blood pressure adjusted for age and sex, using end points from different sources.



In the main analysis all 3 sources of end points are used (primary care, secondary care and death records). To compute endpoints based on secondary care and mortality (second row where applicable) patients were followed up until a hospital admission or death for the specified event, ignoring diagnoses/events recorded in primary care. Similarly, for mortality endpoints patients were followed up until death, ignoring non-fatal presentations. The majority of deaths from stroke are unclassified (not included in the mortality estimate from ischaemic stroke shown here).

Figure S 20 Age and sex adjusted hazard ratios (95% CIs) for 20 mmHg higher systolic blood pressure according to the number of BP measurements taken within 2 years of baseline (1 or more [as in the main analysis], only 1, or 2 or more).

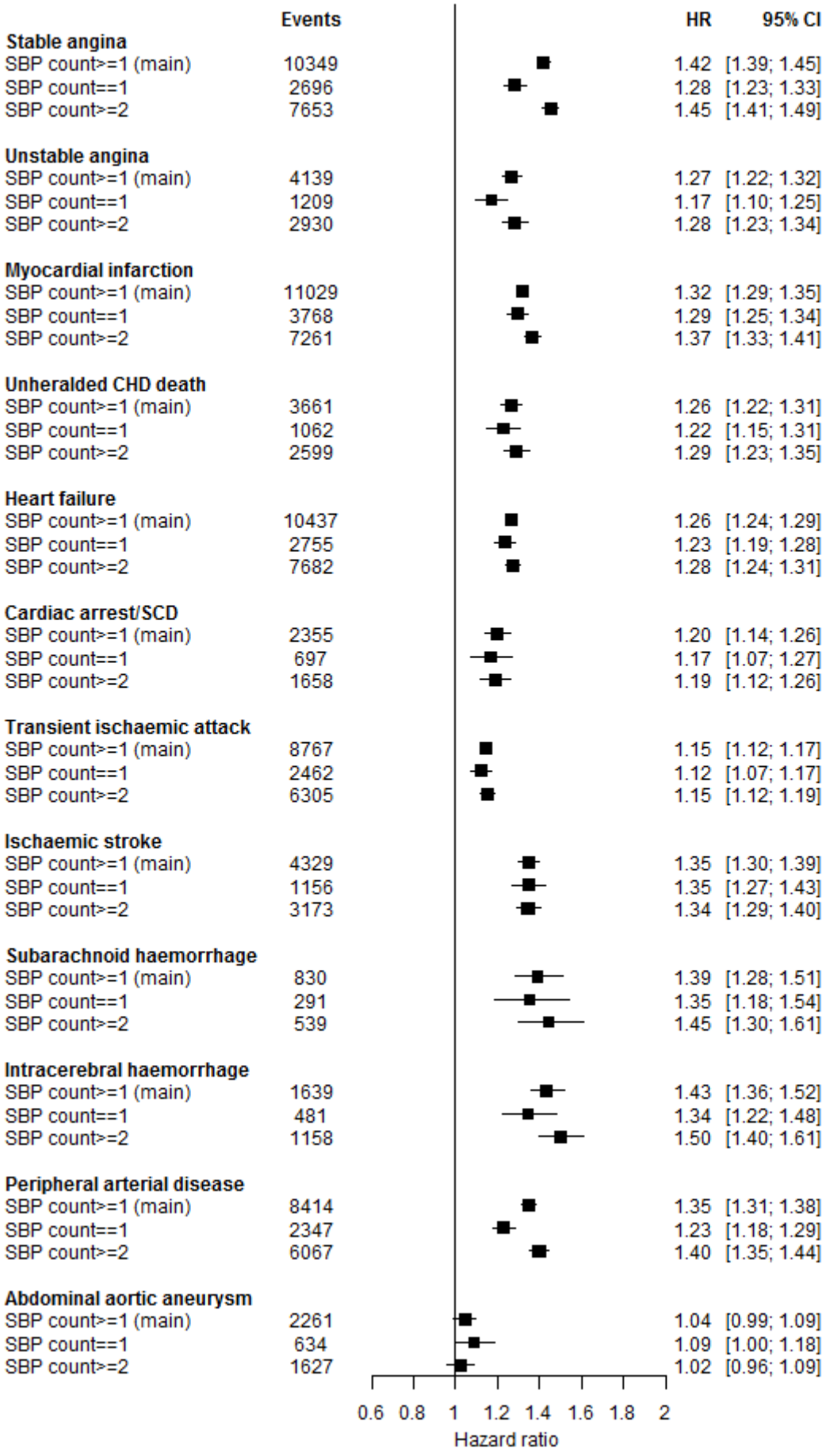


Figure S 21 Age and sex adjusted hazard ratios (95% CIs) for 20 mmHg higher systolic blood pressure based on a single measurement closest to the baseline (within 2 years of baseline).

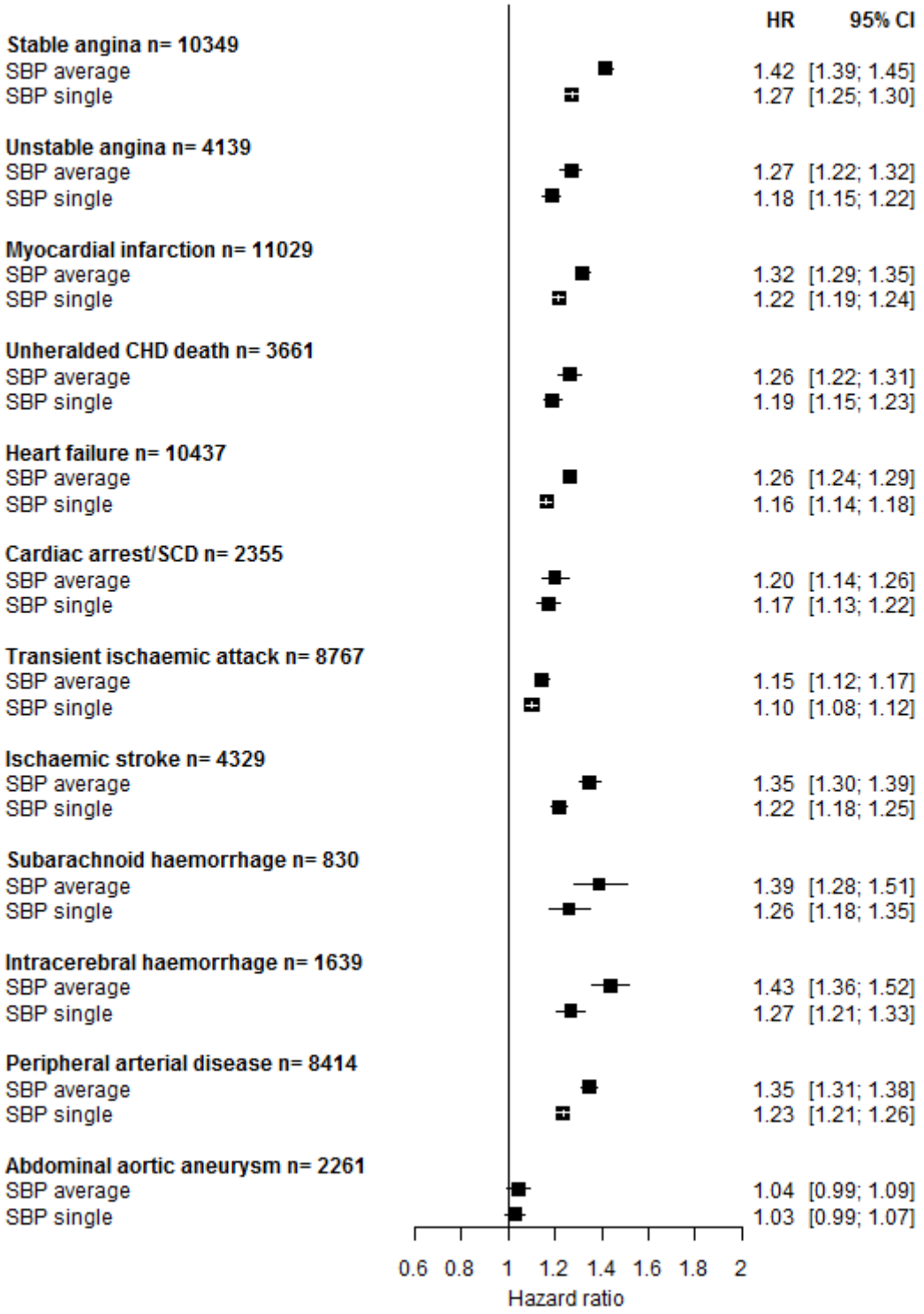
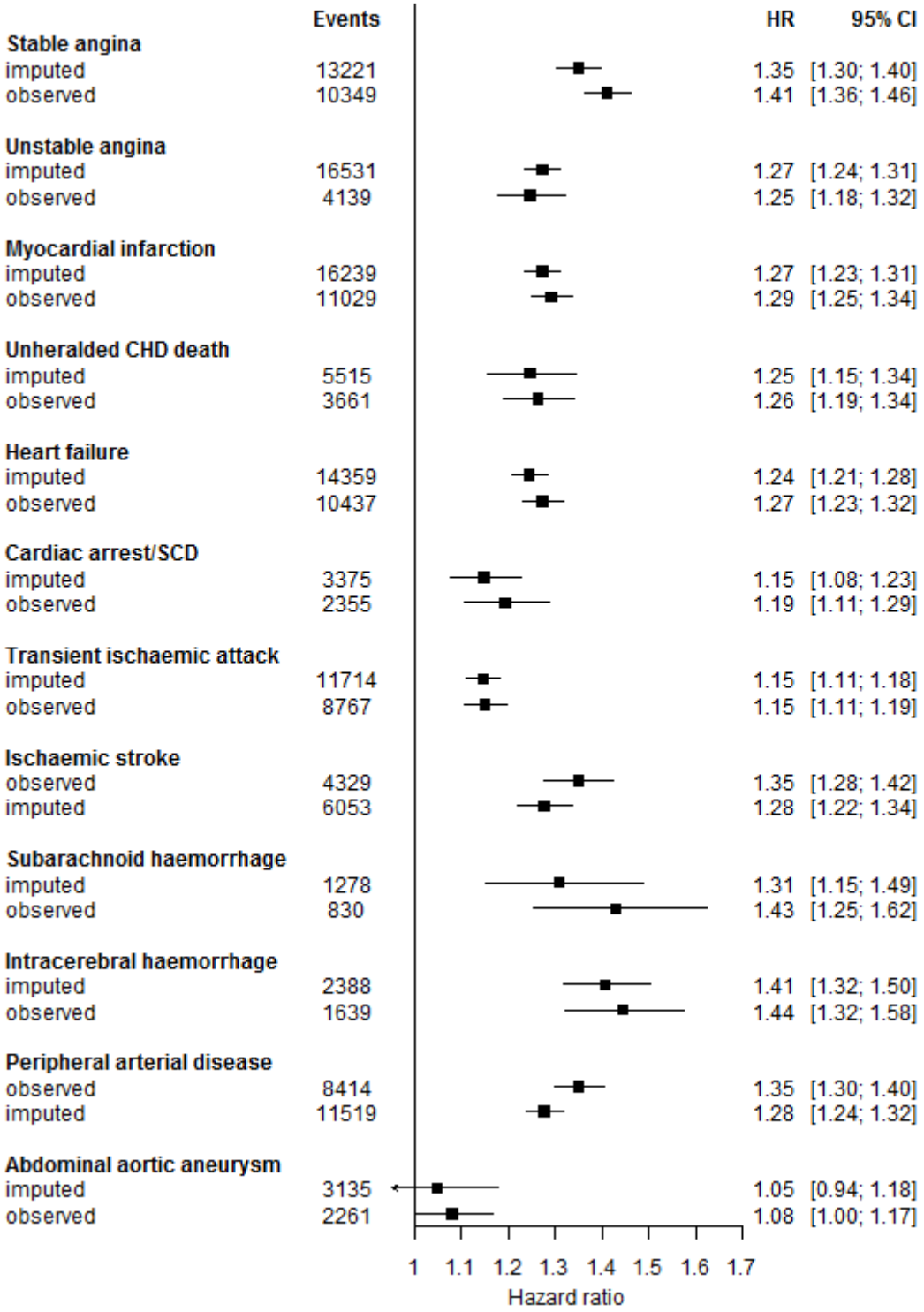


Figure S 22 Age and sex adjusted hazard ratios (95% CIs) for 20 mmHg higher systolic blood pressure based on imputed and observed (main analysis) blood pressure levels.



Dataset including observed and imputed BP, N= 1,937,360 patients; complete cases for SBP (as in main analysis) N= 1,258,006 patients.

Supplementary methods

Multiple imputation

Supplementary methods

Multiple imputation

Multiple imputation[1] was implemented using the *mice* algorithm in the statistical package R. Imputation models were estimated separately for men and women and included:

a) all the baseline covariates used in the main analysis (age, quadratic age, diabetes, smoking, systolic blood pressure, diastolic blood pressure, mean arterial pressure, pulse pressure, total cholesterol, HDL cholesterol, body mass index),

b) prior (between 1 and 4 years before study entry) and post (between 0 and 1 year after study entry) averages of continuous main analysis covariates and other measurements not in the main analysis (white cell count, haemoglobin, creatinine, alanine transferase),

c) baseline medications (statins, blood pressure medications, aspirin, oral contraceptives and hormone replacement therapy),

d) coexisting medical conditions (history of depression, cancer, renal disease, liver disease and chronic obstructive pulmonary disease),

e) the Nelson-Aalen hazard and the event status for each endpoint analysed in the data[2].

Non-normally distributed variables were log-transformed for imputation and exponentiated back to their original scale for analysis. Five multiply imputed datasets were generated, and Cox models fitted to each dataset. Coefficients were combined using Rubin's rules.

We checked whether the imputations were plausible by comparing plots of the distribution of observed and imputed values of all variables. We checked whether the exclusion of patients with no blood pressure measurements (within two years of the baseline) biased the reported associations with cardiovascular diseases by comparing hazard ratios estimated based on imputed data (Figure S22).

Estimation of lifetime risks and years of life-lost

We estimated lifetime risks of each cardiovascular disease adjusted for the competing risk of other cardiovascular diseases and non-CVD mortality based on Cox models with age as the timescale. For a given disease q this involves a) estimating separate Cox models for events of disease q and for the competing events1,…,q-1,q+1,…,Q including the same predictor variables, b) multiplying the hazard contribution for disease q at a given age by the probability of being still at risk and not having experienced a competing event by that age, and c) computing the cumulative incidence (sum of hazards) between the baseline age (age at entry to study) and age 95 ('lifetime').

Thus, for individual *i* the lifetime risk of experiencing disease *q* from baseline age $t_i$to attained aget_i+T in the presence of the competing risks is given by:

$$r_i(T) = \int_{t_i}^{t_i+T} h_{0q}(t)e^{\beta_q x_i}\, exp\left[-\int_{t_i}^{t_i+t}\sum_{k=1}^{Q} h_{0k}(t)e^{\beta_k x_i}du\right]dt \qquad [1]$$

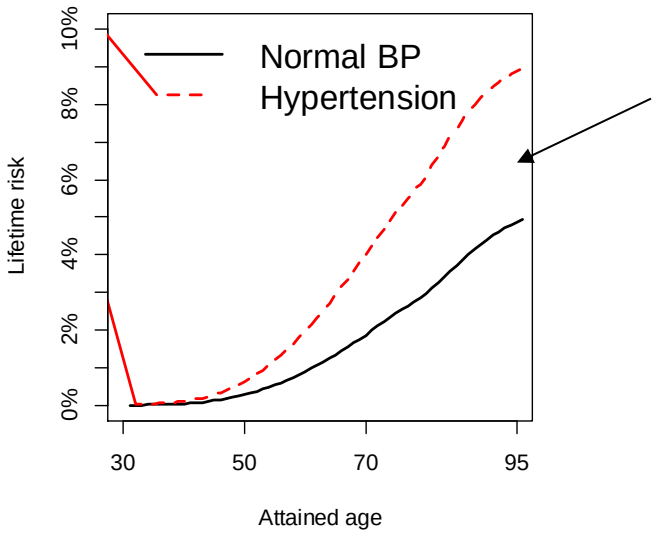
where $h_{0q}(t)$ is the baseline hazard for disease *q* at age *t*

β_q is a vector of coefficients for cause *q*

x_i is the vector of covariates for individual *i*

$h_{0k}(t)e^{\beta_k x_i}$ is the hazard for disease *k* for individual *i* at age t given covariates x_i

Expression [1] is estimated by replacing coefficients and baseline hazards by their estimates. Because the baseline hazard is estimated as a step function, the integrals are replaced by sums over event times.



Diff. in area under the two curves represents years of life lost

Suppose the two curves in Figure S1 represent the lifetime risk of a 30-year old individual with normal BP (black line) or hypertension (red dashed line) at the baseline measurement. The years of life lost (YLL) are estimated from the difference in the area under the two curves, i.e.:

$$YLL = \int_{30}^{95}\{r_N(u) - r_H(u)\}du \qquad [2]$$

where$r_N(u)$ and $r_H(u)$ represent risk estimates up to age *u* (estimated by expression [1] and adjusted for other risk factors (baseline age, sex, diabetes, smoking status, total cholesterol, HDL cholesterol) assuming normal blood pressure or hypertension respectively, averaged over individuals in the data. We estimated {2} by applying the trapezium rule in intervals of u=0.5 years, from the baseline age to age 95.

Reference List

1 Rubin DB. Multiple Imputation for Nonresponse in Surveys. *New York* 1987.

2 White IR, Royston P. Imputing missing covariate values for the Cox model. *Stat Med* 2009;28:1982-1998.

3 Higgins JP, Thompson SG, Spiegelhalter DJ. A re-evaluation of random-effects meta-analysis. *J R Stat Soc Ser A Stat Soc* 2009;172:137-159.